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American Perfumer

HEALTH
SCIENCES

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Pharmacologically active agents in cosmetics

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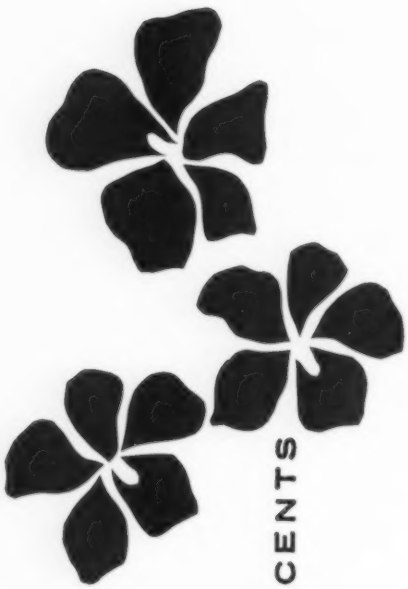

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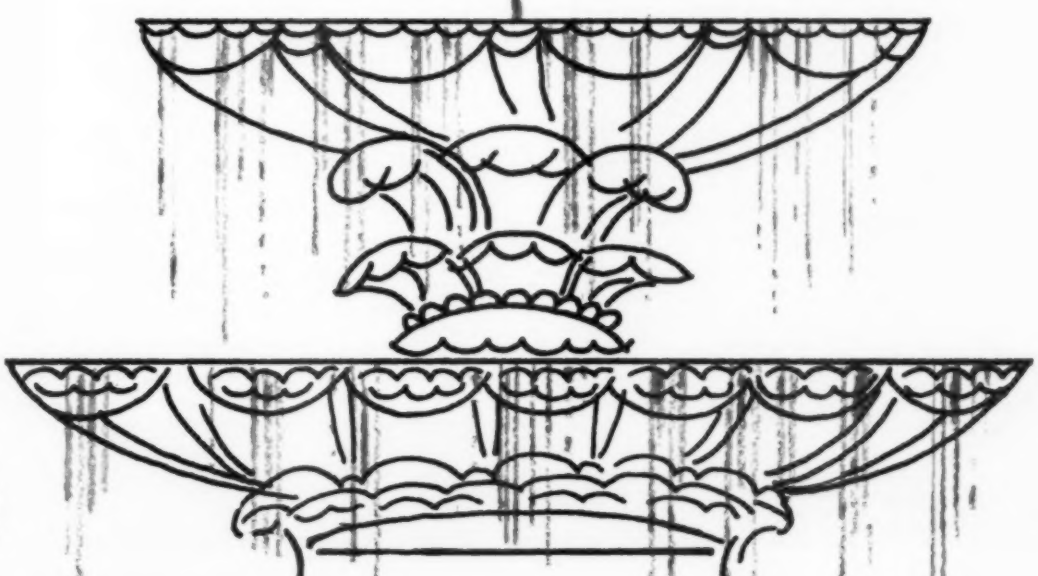

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American Perfumer

VOL. 76, NO. 9 September, 1961

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Inhalt

Pharmacologically active agents in cosmetics ..... *by Dr. Richard E. Faust* 19

In this two-part article, definitions and basic considerations are cited and examples of current trends are set down.

Agents pharmocologiquement actifs sur les cosmétiques

Dans cet article, fait en deux parties, il y est cité des définitions et des considérations de bases. Des exemples sur les tendances courantes y sont donnés.

Agentes Farmacológicamente activos en los cosméticos

En este artículo de dos partes, se citan definiciones y consideraciones básicas y se establecen ejemplos de tendencias corrientes.

Pharmakologisch aktive Stoffe in Kosmetika

In diesem aus zwei Teilen bestehenden Artikel werden Definitionen und grundlegende Erwägungen angeführt und Beispiele für die gegenwärtigen Richtungen gegeben.

The fixative properties of musks ..... *by Dr. J. Sfiras* 27

Author discusses general considerations of the chemical structure of products with a musk-like odor.

Les propriètés odorantes du musc

L'auteur parle des considérations générales de la structure chimiques des produits ayant les propriétés odorantes du musc.

Las Propiedades Fijadoras de los Almizcles

El autor discute consideraciones generales de la estructura química de productos con olor de almizcle.

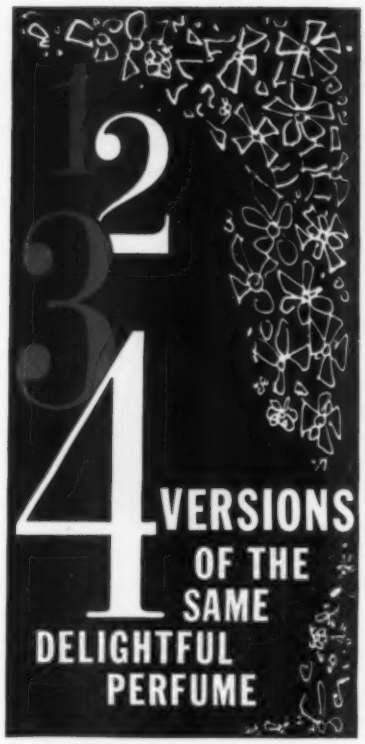
Die fixierenden Eigenschaften von Moschus

Der Verfasser stellt allgemeine Betrachtungen über den chemischen Aufbau von Erzeugnissem mit mit moschusartigem Geruch an.

Use of ion exchange resins in antiperspirant-deodorant preparations 30

The therapeutic value is discussed and several clinical cases are cited. Much of the material is a compilation of reports by the late Dr. Francis M. Thurmon.

Emploi de l'ion, en échange des résines, dans les préparations des déodorants contre la transpiration.



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La valeur thérapeutique en est discutée et plusieurs cas médicau y sont cotés. Beaucoup de ces produits représentent un ensemble des rapports fait par feu Docteur Francis H. Thurmon.

El uso de ion intercambia resinas en preparaciones de desodorantes contra la transpiración

Se discute el valor terapeútico y se citan varios casos clínicos. Mucho del material es una compilación de reportes por el difunto Dr. Francis M. Thurmon.

Anwendung von Ionen-Austausch-Harzen in schweiss—und geruchverhütenden Mitteln

Die therapeutische Bedeutung wird besprochen und mehrere klinische Fälle werden angeführt. Ein grosser Teil des Materials besteht aus einer Ansammlung von Berichten des verstorbenen Dr. Francis M. Thurmon.

The present status of HLB (hydrophile-lipophile balance) ..... ***by Paul Becher*** **33**

Author not only defines what this quantity is, but also makes clear what it isn't.

Les presents statuts de l'EHL (hydrophile—lipophile equilibre).

L'auteur définit la quantité emplyer.

El estado presente del BHL (balance hidrofilo-lipofilo)

El autor no sólo define que es esta dosis, sino que también aclara lo que no es.

Der gegenwärtige Stand HLG (Hydrophil-Lipophil Gleichgewicht)

Der Author erklärt nicht nur, was es ist, sondern auch was es nicht ist.

Activated carbon adsorbs essence to recapture dwindling market ..... ***by Dr. Murray Berdick*** **39**

Recent patented process keeps essence in stable form during transport and permits reconstitution of the material on site.

Le carbone activé adsorbe l'extrait afin d'accaparer encore une fois un marché déperissant

De récents procédés brevetés gardent l'extrait sous forme stable pendant le transport et donne la possibilité de le reconstituer sur place.

El carbón activado adsorbe esencias para recuperar el mercado decayente

Un proceso patentado reciente, conserva las esencias en forma estable durante el transporte y permite la recostitución del material en el sitio de destino.

Aktivierter Kohlenstoff adsorbiert Essenzen, und der schwindende Markt wird zurückgewonnen

Durch den vor kurzem patentierten Prozess werden Essenzen während eines Transportes in beständigem Zustand gehalten, und die Wiederherstellung des Materials an Ort und Stelle wird möglich gemacht.

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Published Monthly by Allured Publishing Corporation. Office of Publication: Pontiac, Illinois. **Editorial and executive offices:** 418 North Austin Boulevard. Oak Park, Illinois. P. W. Allured, President. Subscription Rates U.S.A., Possessions and Canada, $5 one year; $1.00 per copy. Other countries $15 one year. Allured Publishing Corporation is also publisher of The Manufacturing Confectioner.

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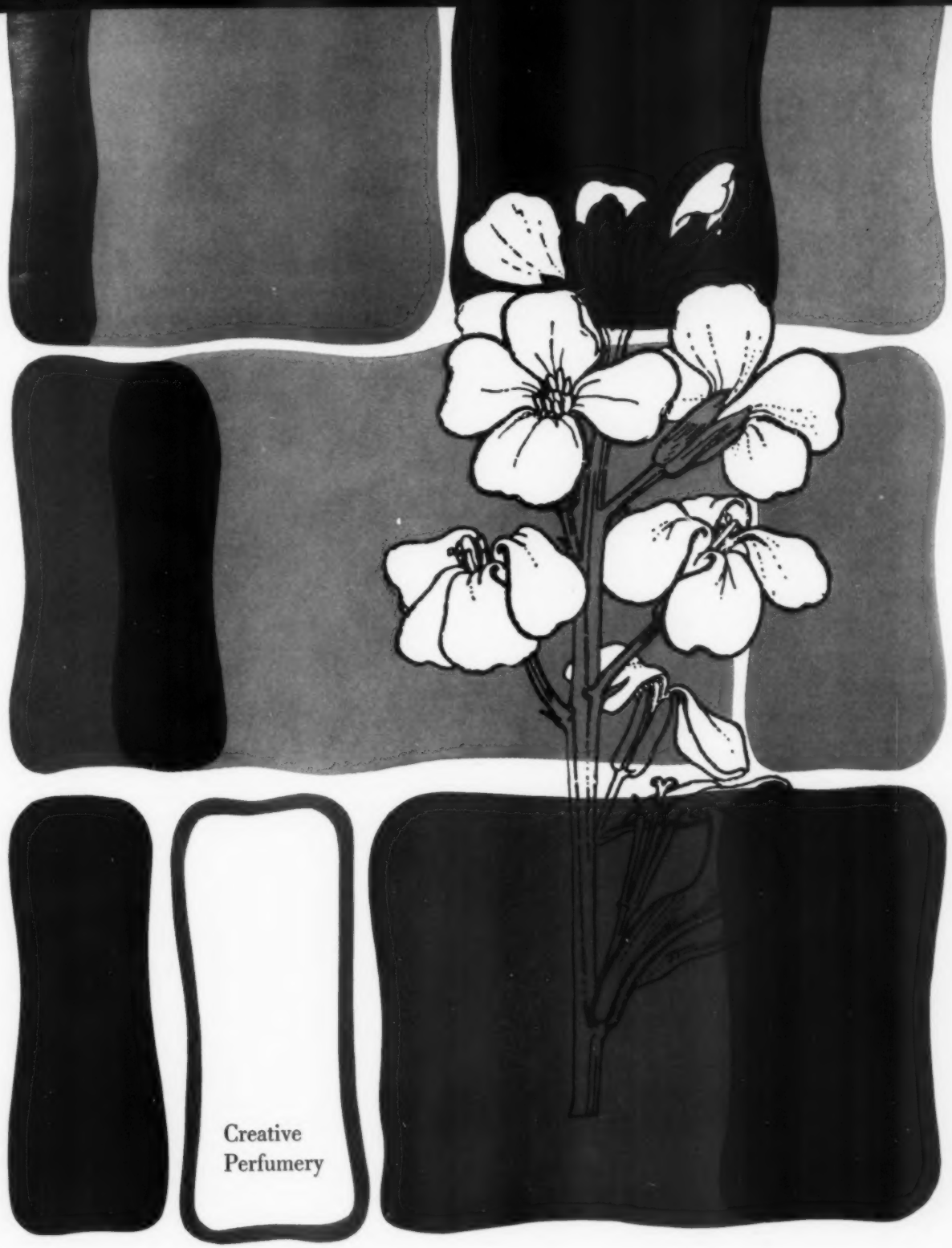

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REACTIONS

Acid-stable glyceryl monostearate

Would you please tell us the difference between the acid-stable grade of glyceryl monostearate and the regular type? In other words, what is added to the product to make it acid-stable?—M. N., Chile.

The ordinary self-emulsifying glyceryl monostearate contains some added potassium stearate as an auxiliary emulsifier. The acid-stable grade contains either a cationic or an anionic surfactant which is not affected by electrolytes to act as an auxiliary emulsifier. A third grade is available which contains no added auxiliary emulsifier. This is often referred to as the pure *glycerol monostearate.*

Facial mask

Would you please give me some idea what a preparation such as Dory's Facial Mask contains? I have determined certain things about it as follows: It contains a carbonate and the pH of this product appears to be around 10. I am particularly interested in knowing what the film-forming material might be that is employed in this product.—O. G., Mississippi.

We obviously do not know the composition of Dory's Facial Mask. We do know, however, that a powdered mask may be made using one of the alginates as the film-forming substances, to which various setting or gelling agents (such as the polyvalent cations) have been added. Sequestering agents (such as the polyphosphates) control rate of gelling.

Cosmetic bleach

There has been an increase in demand for a cosmetic bleach hydrogen peroxide in a liquid cream form. Could you give us, with various formulation, the step by step procedure for producing a cosmetic bleach hydrogen peroxide liquid cream form?—P. Z., Louisiana.

A very interesting discussion of the stable peroxide creams is found in SCHIMMEL BRIEFS, No. 311, published in February, 1961, by Schimmel and Company, Inc., Windsor Highway, Newburgh, New York. We hasten to remind you that the effective peroxide creams mentioned in the Briefs are covered by numerous patents and that you should be careful when using any of the data recommended not to infringe on the patents. Basically, you should make an acid-stable cream from one of the higher alcohols such as cetyl or stearyl containing some sulfonated alcohol. The product, Lanette Wax is of this type. Another material you can use is an acid-stable glyceryl monostearate.

Synthetic resin

We are looking for suppliers of synthetic resin to use as a base for colorless nail enamel. We would be grateful if you could give us names of suppliers.—D. S. L., Iceland

The only synthetic resin with which we are acquainted that has been suggested for possible use in nail polish are the acrylate resins. These may be blended with sulfonamide plasticizers and nitrocellulose of the RS type with the one-half second variety most popular in use. Supplier's names are being sent by letter.

Correction

Your article "Surface Styling Makes Stock Containers Individualistic" which appears on pages 49-51 of the August issue was very interesting but not entirely accurate.

While the two containers which appear at the top of page 50 are perhaps similar, they are not, as your article states, the same stock bottle.

Carr-Lowrey manufactures both containers. The Prince Matchabelli Abano bottle is our stock #100 design in opal glass. The Yardley Flair aerosol is a private mold design which we manufacture for and sell exclusively to Yardley of London, Inc.

Geoffrey R. O'Keefe,
Sales Manager
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Our sincere apologies for this slip-up.—The Editors

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Notes

British Patent No. 838,181 claims that the addition of a "minor" amount of alum to synthetic detergents improves cutaneous properties . . . . Along the same line, U. S. Patent #2,982,739 uses "water-soluble alkali metal salts" of gluconic acid and related acids for the same end result . . . . British Patent 869,448 suggests the use of aliphatic alcohols (1-3 carbons) such as ethyl alcohol as a 3-30% water solution for preserving foods—like chicken.

People interested in glyceryl p-aminobenzoate can now also get it from the Bofors Nobelkrut organization . . . . Aluminum nicotinate is a new skin stimulating (rubifacient) compound available in England (Kaylene Chem. Ltd.) . . . . A new aluminum compound with acid neutralizing and buffering ability has been patented in Japan (4149-1960). It is aluminum glutamate . . . . Off and on we have had requests for the source and price of a-furfuryl mercaptan. While there may be other sources, we find a Belgain supplier offering it at a bit over $27 a pound in 25 kilo lots.

The world is the loser in the passing of Prof. W. T. Astbury, noted for his scientific work on hair and related materials. An obituary written by Kathleen Lonsdale points out that his work received no financial help from the wool secretariat . . . . At the same time, the A.M.A. has enriched its staff as well as enlarged it by appointing Walter G. Fredell as assistant secretary to the Committee on Cosmetics. Good luck Walter! . . . . A new soap germicide is said to be in the offing. Olin-Mathieson is reported to have offered 2-thio-1-pyridine oxide for this purpose some time ago.

Inasmuch as the cosmetic industry uses so much stainless steel in manufacturing its products, it is reassuring to read Arnold Lehman's summary of FDA studies in this area. He states, "Small amounts of the metal components are dissolved when food comes in contact with stainless steel utensils and equipment. The amounts are very minute even under exaggerated conditions. These trace quantities are of no pharmacologic significance. Stainless steel alloys most likely to be used with foods or by the food processing industry are safe." (Assoc. of Food & Drug Officials of the U. S., **25**, No. 3, p. 126, July 1961)

Two new fluoride dentifrices are already on the market. One contains a fluoride and hexachlorophene; the other claims to have a more stable stannous fluoride composition . . . . Frazier and his colleagues have done some work on smoking and prematurity. Indications are that smokers may age more quickly—if they smoke more than one pack of cigarettes a day. Nothing definite yet . . . . The A.M.A. is holding a congress on medical quackery in October. It is hoped that the participants are more open minded in their aims and arguments than Senator Kefauver and his team.

Royal Jelly

The current issue of "Cosmetici, Profumi, Saponi" (June 1961) is entirely dedicated to Royal Jelly (Gelée Royale). Piana reviews the production; Desperrois covers its use in cosmetics; Rovesti does a similar job from a different approach, however; Decourt discusses antiseborrhoeic action on the skin; Schotola goes into the usefulness of royal jelly in acne; Moro gives some formulas for honey perfumes. All this is beefed up with a discourse on re-constituted royal jelly and a five page bibliography.

The papers were presented at various cosmetic group meetings. There is little if anything new. None of the papers can back up statements with controlled human tests that would impress FDA or a bonafide cosmetic scientist. And yet, just because we can't prove something, doesn't mean it isn't there or that it isn't useful. This is a useful over-all review. If your file isn't up to date on Royal Jelly, you should get this issue. Most of the useful references are mentioned but no patents are given.

On alcohol

Maybe I went a little hard on British alcohol last February. Freddy Wells corrects me on the matter of odor. Guess it is better than what I smelled shortly after the end of the war. Anyway, Freddy

is going to show me a sample when I am in London at the end of August. Am going to check other samples of deliveries while there, too.

But this doesn't excuse an enlightened country for using methyl alcohol as a denaturant in toilet articles.

Users of alcohol can still get adequate protection in other ways as Her Majesty's government must know. Nor do you have to use S.V.R. We don't here.

Indeed, I pointed out that Canadian alcohol regulations are far better than those of the U.S.A., although ours are pretty good. Both Canada and the U.S.A. seem to have adequate protection against foreign perfumes without using methyl alcohol.

In the "old days", the starting point in producing alcohol was more important than today. One recalls idealistic references to grape and pear alcohol. I've examined a lot of alcohol (from an odor point of view only) during the past 30 years. A reliable and modern factory produces good alcohol. If shipped in clean *new* drums, it arrives in good shape.

By the way, have you checked the pH of a 50% solution of your cosmetic grade alcohol in *neutral* distilled water, lately? You may be in for surprises.

Book Reviews

Aerosols, Science and Technology, Edited by H. R. Shepherd, 562 pages illustrated and indexed. Interscience Publishers, Inc., New York, N. Y. 1961. Price $22.50.

Pressurized Packaging (Aerosols), by A. Herzka and J. Pickthall, second edition, 509 pages, illustrated and indexed. Butterworth and Co., London 1961. Price 70 shillings, (approx. $10.00).

The almost simultaneous appearance of the first revision of Herzka and Pickthall's *Pressurized Packaging*, and *Aerosols, Science and Technology* edited by H. R. Shepherd makes it possible to compare the two books in numerous ways.

The British book by Herzka and Pickthall is in its second edition and revision. It enables the authors therefore, to correct mistakes and omissions which appeared in the first edition. But besides this, one is also aware of the fact that the Shepherd book containing 562 pages covers essentially the same subject matter found in the Herzka and Pickthall book in 509 pages. The Interscience book is priced at $22.50 whereas, the British book is priced at 70 shillings which is approximately ten dollars. Granted that there are differences in printing costs in the two countries, this spread seems quite significant although obviously the authors have nothing to do with setting the price of books they write.

The British book is by far the more international in scope, discussing ingredients, containers, valves and closures.

The British book discusses the history of aerosols and their components in 135 pages while the U.S. book requires 238 pages; propellents are given only 25 pages in Shepherd's book while Herzka and Pickthall take 65 pages. Fiero, a contributor to Shepherd's book, takes 31 pages to discuss pesticides while the British authors take 25 pages. Coating and household specialties require 42 pages in Shepherd's book while Herzka and Pickthall do it in 58 pages.

In a book written by 19 co-authors, as in Shepherd's work, it is practically impossible to prevent duplication. Sometimes this duplication is allowed by the editor to stress a particular point or formulation. However, the extreme repetition "foam overrun" seems careless. The same applies to illustration of identical products in different parts of Shepherd's book.

Editor Shepherd, a specialist in commercial filling of aerosols, apparently failed to get an author to write such a chapter, assuming he was unable to do so himself. This is a notable omission. This phase of the work is well covered by Herzka and Pickthall.

It is known to any book editor, that portions of the material which will appear in his book will have been written several years before publication, while some of it will have been written almost at press time. Yet, it is unforgivable to show sales graphs drawn to include 1959, yet show data terminating in 1957. Although data is always outdated shortly after publication, in this case, it was outdated long before publication. Herzka and Pickthall have the advantage here in that they were able to revise their book in three years after the original edition appeared.

One might comment on the Herzka and Pickthall book that there is a bit of inconsistency in the naming of propellents in different portions of the book. Sometimes they are referred to by number and sometimes they are referred by trade name. On page 294, item 5, odoriferous is misspelled. The terms Ethanol, Ethyl alcohol and alcohol are used interchangeably when either one of the three should have been selected and used throughout.

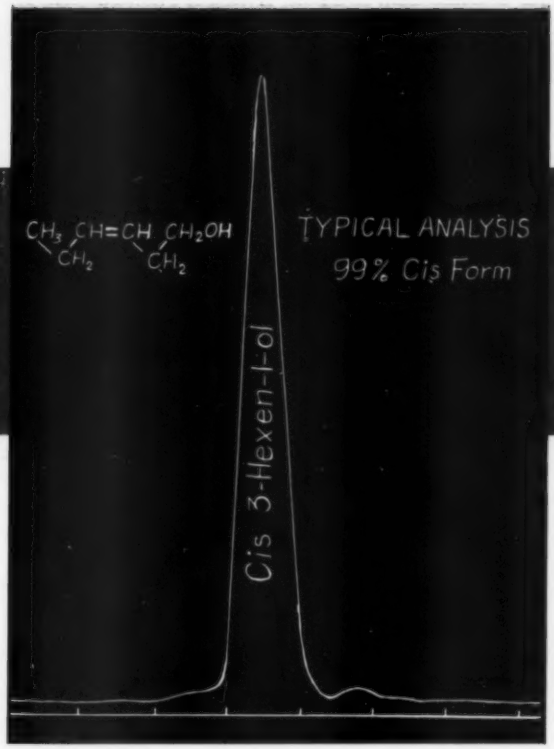
In the case of the Shepherd book, William Knapp and Ray Stetzer are named in the list of contributors and editors but chapters over these names are not found in the book. Of course, editors don't always contribute to a book they are editing, although they usually do.

Of the two books, the British book is the most up-to-date and the best value for the money. Yet, this reviewer can't see how any responsible aerosol laboratory can afford to be without either of them. (M. G. deN.)

Abrege de Cosmetologie Pratique, by Paul Larrieu, 73 pages, 22 Rue Caumartin, Paris 9, France.

This book is almost too small for the material it covers. Some 63 references are found in the book. Only one U. S. reference to Thelma Warshaw, spelled WAISKAM.

The book, abridged as it is, is intended for the pharmacist to guide him in knowing something about cosmetics. (M. G. deN.)



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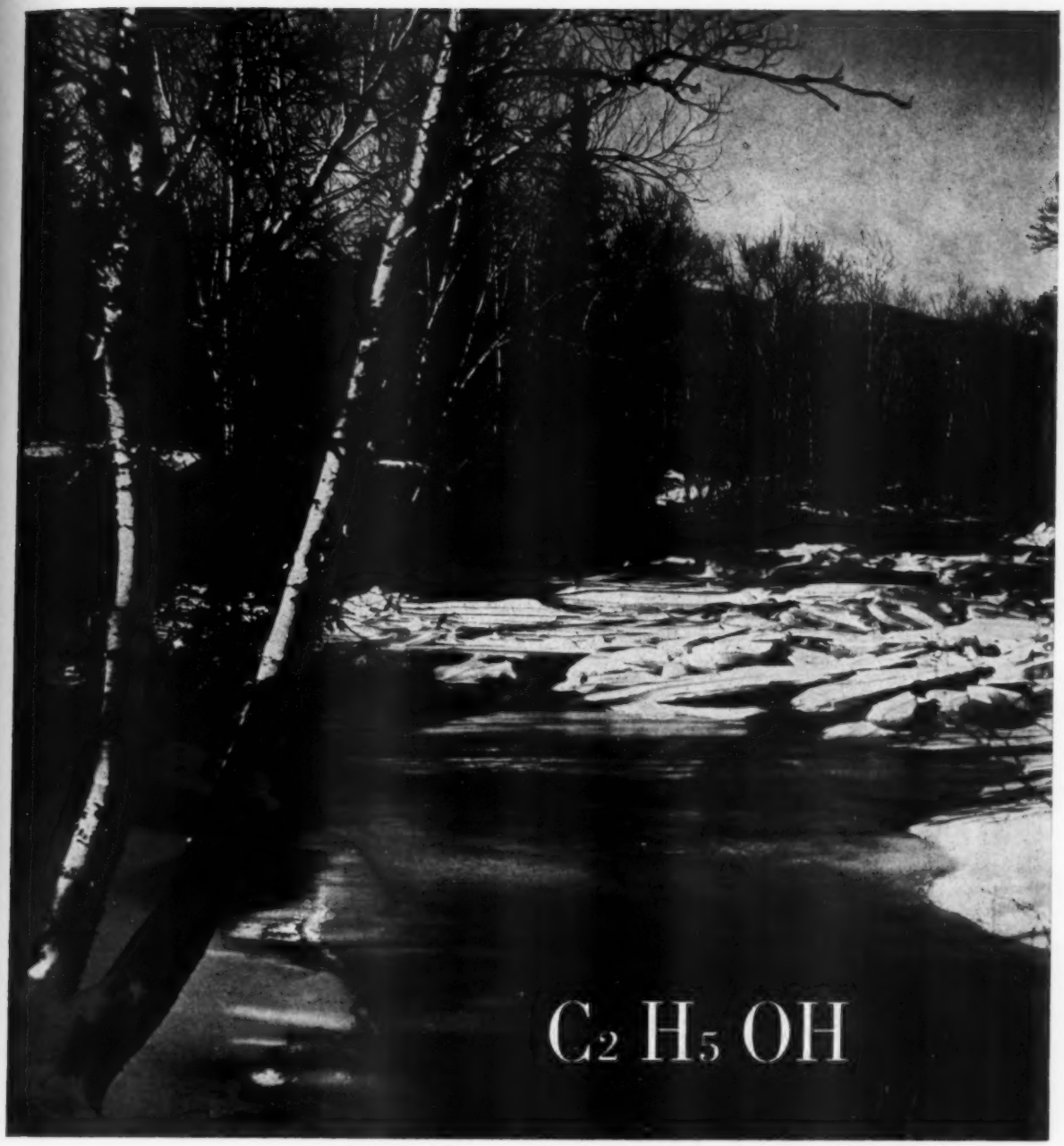

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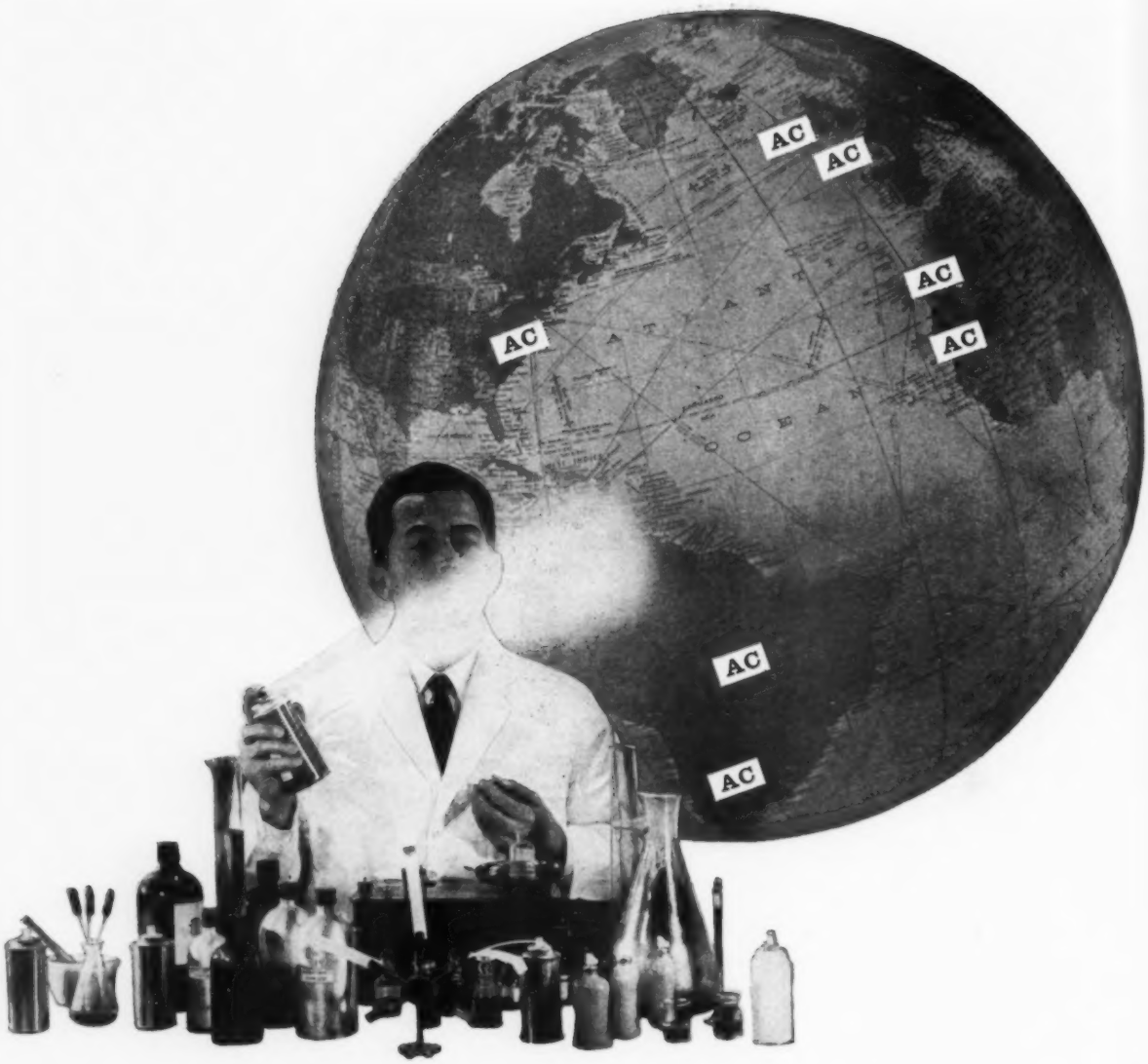

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American Perfumer

SEPTEMBER • 1961
VOLUME 76 NO. 9

Pharmacologically Active Agents in Cosmetics

Part I. — Some Definitions and Basic Considerations

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Introduction

HARRY[1] HAS NOTED that cosmetic preparations may exert a fourfold action, namely; decorative, psychological, social, and clinical. The latter category suggests the use of agents having pharmacological action in cosmetic products and, indeed, there seems to be a trend in this direction. Some criticize this development and consider it fraught with danger[2].

Others, however, argue that the objective of many topical drug products and cosmetics is essentially similar; that is, the restoration and maintenance of a healthy integument, and that as long as no direct hazards are involved in the cosmetic use of active agents, the trend is logical and beneficial. It must be emphasized at the outset that the objective of this article is not to promote or to reject the use of pharmacologically active drug products in cosmetics, but merely to examine this trend, emphasize what may be several important considerations, and attempt to predict future developments. It is not within the scope of this paper to debate the philosophy, legality, or propriety of this question, but merely to present some observations.

If one attempts a literal interpretation of the definition for a drug and a cosmetic given in the Federal Food, Drug and Cosmetic Act, he encounters a rather perplexing situation. Articles used in the "diagnosis, cure, mitigation, treatment, or prevention of disease" are considered by this definition to be drugs; but many cosmetics also function to protect the skin from environmental hazards that would cause pathological changes in the skin. This action may be considered the prevention of disease. We cite the example of an emollient protective hand lotion which when used regularly during the winter exerts a prophylactic action preventing the development of dry, chapped, fissured skin. Lip ices are used to treat and to prevent roughened, chapped, and irritated lips; sunscreens prevent damaging thermal burns.

A cosmetic, as defined, refers to a product for "cleansing, beautifying, promoting attractiveness, or altering the appearance." Drugs, on the other hand, are described as "articles intended to affect the structure or any function of the body."

Now, when even the simplest cosmetic formulations function to cleanse, beautify, promote attrac-

tiveness, or alter the appearance, the structure and/or physiology of the skin is often affected to some degree. A simple preparation of the vanishing cream type, for example, may provide a semi-occlusive film on the cutaneous surface which produces physical change in the integument, such as an increase in the water content of the stratum corneum. The suppression of evaporation causes swelling of the cells in the horny layer and may even promote greater penetration of any drugs incorporated in the vehicle.

Considered in the broadest sense, therefore, all cosmetics alter the structure and/or function of the body to some extent except perhaps those used solely for coloring or fragrance purposes.

Drug or pharmacological action, therefore, is quantitative as well as qualitative and it is the extent of this action that frequently determines whether or not a product should be classified a drug, a cosmetic, or both. Moreover, if a cosmetic product were completely inert and possessed no pharmacologic action it would be useless in many cases and, thus, subject to regulatory action, especially if claims exceeded the actual effects obtained.

There are many products which are classified by law as both a drug and a cosmetic, such as antiperspirants, sunburn remedies, and antidandruff preparations. In other instances, the nature of the labeling claims determines whether the item will be considered a drug or a cosmetic.

The importance of the cosmetic vehicle

When examining the overall subject of pharmacological activity in cosmetics, we must accent the importance of the vehicle or base which in itself can promote beneficial changes in cutaneous structure and functioning. This may be called non-specific treatment in contrast to the specific action of medicinals. Indeed, in the treatment of skin diseases, the vehicle remains of importance at least equal to that of the incorporated drug[3]. Many vehicles are created to accomplish more than merely color, cover blemishes, or provide pleasant fragrance. Such vehicles exert a more hygienic effect by improving the health and suppleness of the skin, often by helping to restore normal physiological equilibriums. The physicochemical actions of the cosmetic base or vehicle include relieving dryness through a semi-occlusive film barrier, protecting the skin from damaging external influences, removing excess keratin or sebum, altering the blood supply to the skin, and alleviating mild pruritus and local discomfort.

The selection of the vehicle is also important, for alcoholic solutions, greasy ointments, anhydrous water-miscible bases, and emulsified creams or lotions (O/W or W/O) have different characteristics with regard to emollient, cooling, lubricating, protective and penetrating properties. A vehicle which promotes too rapid penetration of estrogenic hormones, for example, can cause untoward systemic reactions. On the other hand, the vehicle used to carry the active agent to the skin must not inactivate the agent or prevent its release. For example, certain cationic salts, such as alkaloidal salts, may be incompatible with anionic emulsifiers.

Furthermore, one must constantly recall that topical products change physically after they are applied to the cutaneous surface[4]. As water evaporates from an O/W emulsion, for example, active agents become concentrated. If the active agent is a water soluble drug, it may crystallize and deposit in the oleaginous residue as the aqueous phase evaporates. We must recognize that the actions of drugs may be altered considerably by the vehicles which bring them in contact with the skin.

In view of the outstanding progress of the cosmetic industry in developing and using esthetically pleasing and functional vehicles, it is somewhat surprising to note that certain official ointment bases, such as White Ointment U.S.P. and Yellow Ointment N.F., have remained unchanged. These bases and certain others used in commercial topical pharmaceutical preparations are heavy, greasy products which form an occlusive film that impedes normal skin respiration and gives an uncomfortable feeling of warmth. Such bases do not mix easily with active agents and many prevent continuous contact of the agent with the cutaneous surface.

Of course, there is no ideal vehicle suitable for all drugs, but a most versatile and useful one is an oil-in-water emulsion that spreads easily and leaves a semi-occlusive film which enables the drug to maintain contact with the skin.

On the whole, however, the pharmaceutical industry is tending more and more to consider the importance of cosmetic appeal in topical therapeutics. An excellent example of this trend is in the treatment of acne, where the value of flesh-tinted covering agents and pleasant fragrance has been recognized.

Official drugs used in cosmetics

Now by definition a drug also includes "articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary." If we examine these official compendia, we note that a large number of drugs are common components of various cosmetic formulations. Many of these drugs possess no marked specific pharmacological action and are used in cosmetics as suspending agents, thickeners, stabilizers, humectants, emulsifiers, etc. to create stable formulations with the desired physical characteristics.

This does not mean, however, that in their action on the skin such agents are pharmacologically inert. Included in this category of agents which are used to create the cosmetic vehicle and which may possess a non-specific though oftentimes beneficial action on the skin are the following:

humectants, such as Propylene Glycol U.S.P., Sorbitol Solution U.S.P., and Glycerin U.S.P.;

emulsifiers and wetting agents, such as Polyoxyl 40 Stearate U.S.P., Sodium Lauryl Sulfate U.S.P., Polysorbate 80 U.S.P., and Dioctyl Sodium Sulfosuccinate N.F.;

suspending agents, thickeners, and stabilizers, such as Methylcellulose U.S.P., Spermaceti U.S.P., Stearyl Alcohol U.S.P., White Wax U.S.P., Bentonite U.S.P., and Glyceryl Monostearate N.F.;

preservatives, such as Propylparaben U.S.P. and Methylparaben U.S.P.;

and **other valuable raw materials used in cosmetic formulation,** such as Cetyl Alcohol N.F., Oleic Acid U.S.P., Talc U.S.P., Hydrous Wool Fat U.S.P., White Petrolatum U.S.P., Triethanolamine N.F., and Stearic Acid, U.S.P.

In discussing the action of cosmetics containing specific and relatively active pharmaceuticals, one must be cautious about loosely using terms to describe the action of such products. For example, the term "stimulating" may mean vasodilation, as seen in the use of some mild rubefacients in hair lotions; it may refer to an increased rate of proliferation of epidermal cells, as reported from the use of allantoin; or it may simply describe the refreshing and cooling sensation following the use of an after-shave lotion containing menthol.

With this thought, let us review some official pharmacologically active agents used in cosmetics. Table 1 presents various pharmacological classifications with examples of some official U.S.P. and N.F. drugs currently being used in cosmetic formulation.

Table 1.
Classes and examples of some official U.S.P. and N.F. drugs used in cosmetics.

Antimicrobial substances

Tyrothricin N.F.	Bithionol U.S.P.
Thymol N.F.	Neomycin Sulfate, U.S.P.
Salicylanilide N.F.	Chlorobutanol U.S.P.
Phenylethyl Alcohol N.F.	Hexachlorophene U.S.P.
Gramicidin N.F.	Benzethonium Chloride, U.S.P.
Chlorothymol N.F.	Boric Acid U.S.P.
Cetylpyridinium Chloride U.S.P.	

Astringents

Zinc Phenolsulfonate N.F.	Zinc Chloride N.F.
Alum N.F.	Hamamelis Water N.F.

Local Anesthetics and Antipruritics

Butyl Aminobenzoate N.F.	Menthol U.S.P.
Benzyl Alcohol N.F.	Camphor U.S.P.
Ethyl Aminobenzoate N.F.	

Emollients and Lubricants

Cetyl Alcohol U.S.P.	Hydrous Wool Fat U.S.P.
Petrolatum N.F.	Olive Oil U.S.P.
Sesame Oil U.S.P.	Cottonseed Oil U.S.P.

Keratolytics

Salicylic Acid U.S.P.	Resorcinol U.S.P.

Local Irritants

Arnica N.F.	Pilocarpine Hydrochloride U.S.P.
Resorcinol Monoacetate N.F.	

Other Agents

Estradiol N.F.	Precipitated Sulfur U.S.P.
Betanaphthol N.F.	Ammoniated Mercury U.S.P.
Benzoin Tincture N.F.	Diethyltoluamide U.S.P.
Benzoic Acid U.S.P.	

Safety factors in use of pharmacological agents

In evaluating the safety factor when selecting and using pharmacological agents, one must keep in mind that cosmetics are often used for long periods of time and by all age groups with various types of skins and constitutional differences in susceptibility to untoward reactions. People also vary markedly in their use of cosmetics with respect to frequency of application, quantity applied, and extent of inunction.

The possibility of synergism or potentiation which may occur among agents in the formulation or with other products the person may be using concomitantly must be considered. Also, because of the medicated factor, there may be a tendency to use the cosmetic in conditions where the skin is damaged and, thus, penetration and the possibility of adverse side effects will be increased[5]. Furthermore, if cosmetics move toward the area of self-medication, the danger of masking or modifying symptoms of serious pathology becomes a factor with which cosmetic chemists must be concerned.

When various pharmacologically active materials are added to cosmetics, the incidence of untoward consumer reactions, such as sensitization, may increase. Thus, it would perhaps be well to consider the more widespread use of warning statements that such products are to be discontinued if they produce irritation after application. The Food and Drug Administration has outlined a number of warning statements, some of which apply to topical products[6]. The warnings of interest to cosmetic manufacturers include those for antiperspirants, antiseptics for external use, mercury preparations, sulfur preparations, and zinc stearate dusting powders.

In order to minimize the incidence of untoward cutaneous reactions in the use of any cosmetics, one should attempt to formulate a product of maximum simplicity regarding the number of components used. Furthermore, by the addition of various pharmaceutical agents, one can create medicated cosmetics which are more functional and useful, but he must be certain that the added products do not introduce factors which may be deleterious from a standpoint of allergy or other toxic manifestations. The beneficial effects obtained must always be weighed against the potential hazards involved. Although objectionable side effects may be tolerated in the use of potent drugs in order to obtain maximum therapeutic response in pathologic states, such adverse effects should not be tolerated in a product designed essentially for cosmetic purposes.

Using and evaluating pharmacological agents

The evaluation of pharmacological action in cosmetics is oftentimes difficult, especially as one moves from *in vitro* techniques to *in vivo* tests and clinical studies. Reports may vary and investigators frequently differ in their conclusions regarding the efficacy of a product to alleviate, correct, or prevent a particular skin condition. There has been considerable discussion concerning the mandatory pretesting of cosmetic formulations to demonstrate safety. With the increasing use of pharmacologically active agents in cosmetics, adequate data to show not only safety but efficacy is necessary and all reputable companies would undertake such an evaluation program before introducing a new product of this type. It is, of course, essential also that when novel agents having specific pharmacodynamic activity are used in cosmetics, accurate and efficient assay procedures be developed.

When considering the action of topically applied agents, one must be aware that there may be a systemic as well as a local effect. Therefore, we must be concerned with percutaneous absorption. Oftentimes, however, there is a degree of over-emphasis of the importance of percutaneous absorption and it is frequently forgotten that this effect is, in most instances, unnecessary and even undesirable. Certain-

ly in the use of antimicrobials, for example, one is concerned with the penetration of the agent into the cracks and crevices of the skin where it can exert its action, but absorption through the skin is not necessary and may even produce toxic systemic reactions. In estrogen-containing cosmetics, as we have noted before, a vehicle, such as alcohol, which promotes rapid passage of the hormone through the skin is undesirable.

The function of a cosmetic

In dermatology, specific therapy directed toward the removal of the source of the disease can rarely be instituted and, therefore, local therapy is frequently designed to alleviate certain symptoms while the skin is returning to normal. Similarly, the physicochemical or pharmacological action obtained with the use of many cosmetics emphasizes the protection of the skin and the restoration of normal physiologic functioning. Although many cosmetics are designed to color, lubricate, cover, or clean the skin, many cosmetic chemists feel that in order to have truly useful and effective preparations, they must create cosmetics which possess more than eye appeal, a pleasant fragrance, and good stability.

There is an indissoluble union between beauty and health. Cosmetics are concerned more and more not only with accentuating and highlighting normal skin beauty, but also with the restoration and maintenance of skin health. In general, cosmetics possessing pharmacological activity are designed to treat mild deviations from the accepted norm, rather than marked abnormalities. However, it is often difficult to define or to delineate precisely what is normal and what is abnormal. For example, is aging of the skin normal? And, can we actually measure skin aging? Furthermore, it has been stressed by some that the cosmetic industry should not create therapeutic cosmetics, but should develop products to counteract or camouflage the slight but unpleasant shortcomings of the skin. Again, what exactly do we mean by slight shortcomings, and who decides what is unpleasant?

In the evolution of cosmetics from an art to a science, efforts were directed to produce excellence in regard to stability, uniformity, and safety of raw materials, as well as to the perfection of the esthetic qualities of color and fragrance. Now, however, many feel that cosmetic science has reached a second stage, described by some as preventive medicine, when products are created to fulfill a physiological or therapeutic requirement.

Summary

Because of the indissoluble union between beauty and health, more and more cosmetic products are being formulated with active pharmacological agents to help restore and maintain a healthy integument. Many feel that this is a natural development, but one that may possess hazards if various precautions described are not followed.

It is frequently difficult to distinguish between drug action and cosmetic action in topical preparations. Oftentimes, a simple cosmetic vehicle may exert a beneficial effect on the skin through physicochemical mechanisms which are non-specific pharmacologically, yet which do alter to some degree skin structure or function. Such an effect may be as important to the restoration of normal cutaneous physiology as that produced by a potent and specific pharmacological agent. In describing pharmacological action, therefore, one must keep in mind that most products applied to the cutaneous surface alter the structure or functioning of the skin, even though this may be slight in some cases. Thus when attempting to differentiate between drug and cosmetic action, it is essential that one recognize a quantitative as well as a qualitative factor in describing pharmacological activity.

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Part II. — Examples of Current Trends

Introduction

DURING THE PAST THIRTY YEARS we have witnessed a dramatic increase in the use of cosmetics, including more recently, those containing pharmacologically active agents. It is possible in this brief survey to review only a few of the most prominent examples of these agents. It must be emphasized at the outset, also, that the object of this paper is neither to support nor to discredit the use of agents classified as drugs or medicinals in cosmetics, but merely to report the current trend and to predict possible developments.

The term "active ingredient" has been used rather loosely in cosmetics. In a broad sense all components of a topical formulation have a specific action or function and contribute to the over-all effectiveness of the product. Some ingredients may act as solvents, diluents, preservatives or colorants, while others are included to provide fragrance, coverage, luster, firmness, or adhesion. Many such components of the cosmetic vehicle affect the cutaneous surface favorably and provide what might be called a non-specific effect. For example, various oils, waxes, fatty alcohols, and related substances may form a semi-occlusive or occlusive emollient film over the skin which protects the cutaneous surface from external irritants and contributes to proper hydration of the stratum corneum.

We are primarily concerned in this survey, however, with agents reported to exert a more specific and often greater pharmacological effect on the skin which is being adversely influenced by either the internal or external environment or both.

Botanicals

The treatment of skin disorders with whole plants or various plant extracts and constituents can be traced to antiquity. Through the years many agents from the vegetable kingdom have been used in cosmetic products, including, for example, alkaloids (pilocarpine, quinine), carbohydrates (acacia, tragacanth), tannins (tormentilla), essential oils, glycosides, and resins. Such botanical substances have been employed to produce a hyperemizing effect, promote granulation and epithelization, provide astringency, protect the cutaneous surface, or exert a stimulating action.

Janistyn[1] recently discussed the active principles of plants used in cosmetics, including those producing an estrogenic effect.

Schwarz[2] has reviewed the various botanicals taken internally to achieve a cosmetic effect, as well as those applied externally, such as quinine, cinchona, hamamelis, and St. John's wort. The activity of many such plant materials is due to their tannin content which exerts an astringent effect on the skin. One of the most widely used astringent plant products in cosmetics is hamamelis, commonly known as witch hazel [3,4].

Azulene, the effective principle of chamomile flowers, has been promoted for use in cosmetics as an antiphlogistic and anti-inflammatory agent[5]. The azulenes which are important pharmacologically are cham-azulene and quai-azulene[6]. The exact mode of action of these agents is still unknown, but their beneficial influence is said to be due to an effect on histamine[7].

Ginseng root has been used internally as a stimulant, aromatic bitter and heart tonic, and recently, its use in cosmetics has been promoted. Active principles said to be 90 to 100 times more potent biologically than the root proper have been isolated by chromotography[8]. Yamada[9] isolated and purified panaquillon, panacen, and panaxic acid from Chinese ginseng and these agents were capable of elongating the sexual cycle in mice. A pantothenic acid-like factor has been found in high concentration in various crude drugs used as tonics, including ginseng[10].

Applying Filatov's principle to plants, Rovesti[11] has described the production of special kinds of tissue stimulants of plant origin called phytostimulins. When applied to human tissues, these agents are said to exalt the vital processes and increase the defensive capacity. Various phytohormones and auxins have also been evaluated for beneficial effects in cosmetics. Auxin A, auxin B, 2,4-dichlorophenoxyacetic acid, and 2,4,5-trichlorophenoxyacetic acid are reported to regenerate muscular tone in wrinkled skin and in other ways to be stimulating and activating to the skin[12, 13].

Cucumis sativus (cucumber) juice has been added to cosmetic creams and lotions for some time, especially in Europe. Recent studies have shown that various extracts of cucumber possess enzyme dehydrogenation activity[14], a high concentration of vegetable pectin[15], antibacterial activity against S. aureus and E. coli[16], free ribonucleic acid[17], and various active chemicals, including hydroxycinnamic acid[18].

Bialeurone is a concentrated distillate of aleurone extract, a material obtained by a biological process from wheat. Its amino acid, vitamin, and mineral content have been reported and it has been said to stimulate the general nutrition of the skin when it is injected or applied exernally[19].

Glycyrrhetinic acid, a sapogenin derived from licorice root, has been compared with hydrocortisone and found to possess unusual antiphlogistic and anti-inflammatory properties[20]. New organic derivatives of glycyrrhetinic acid which are more soluble in body fluids and thus more effective locally, have been patented[21]. Other compounds obtained from licorice root, such as xanthoglabrol, have been shown to possess anti-inflammatory activity[22].

The possible use in cosmetics of pollen extracts to aid cellular metabolism and regeneration of the epidermis has been discussed[23, 24]. Other materials of plant origin suggested for use in cosmetics and reported in the recent literature include avocado oil[25], alfalfa liquid[26], the juices of germinated corn and lupine seeds[27], and in India the fresh juice of the flowers of Taberna Montana Coronarium[28].

Biologicals

Recent work in the biological sciences has sparked research in the use of tissue extracts and related substances in cosmetic products, but results, though promising, have not been conclusive. The studies of Filatov and associates on the properties of various biological fluids has stimulated interest in tissue and serum therapy in cosmetics[29]. Filatov's theory proposes that during stress the tissues are capable of producing defense substances possessing marked stimulating and rejuvenating properties. Emphasis has been placed on animal tissues associated with active cell proliferation, such as the placenta and various parts of the growing embryo. It has been claimed that the application of such extracts improves the general tone and health of the skin. Alkaline phosphatase activity has been used to standardize human lyophilized placenta extract[30].

The significance of understanding the importance of amino acids and proteins and their relationship to a healthy integument has been stressed[31]. The protein balance of the skin is said to be important not only in tissue growth and production of specific proteins, enzymes, and hormones, but also for the maintenance of a normal, properly hydrated and nourished skin. Amino acids in cosmetics represent nitrogenous substances capable of providing exogenous nourishment of the skin and thus maintaining the skin's normal protein balance[32]. Furylglycine and its intermediate, 5-furylhydantoin, have a hydrating, tonefying, and smoothing effect on tissues[32]. Tryptophan, which appears to be the base for 5-hydroxytryptamine, has been proposed for its possible restorative effects on aging skin[33]. Since methionine may be able to replace cysteine completely, its potential value in dermatology and cosmetics has been

reviewed[34]. Certain amino acid and polypeptide mixtures are said to help keep the hair in good condition[35].

The importance of enzyme mechanisms in cutaneous physiology is well established and the use of various enzymes or enzyme inhibitors in cosmetic products is plausible. The relationship of hyaluronidase and cosmetic penetrating action has been discussed[36]. Various synthetic antiautolysines (Jaudas agent) have been reported effective in deodorizing perspiration and decreasing skin sensitivity to certain face creams[37].

There are many substances which act as enzyme inhibitors to decrease acid production by dental plaques and some of these have been incorporated into dentifrices[38]. Sodium N-lauroyl sarcosinate is a popular enzyme inhibitor used in dental products to reduce caries. It is possible that certain enzymes of the general type now used in the treatment of certain skin disorders may be of value in various cosmetic products. These include, for example, trypsin, chymotrypsin, papain, streptokinase, and streptodornase[39].

Antimicrobial substances

The use of antibacterial and antifungal agents in cosmetics has increased significantly in recent years, chiefly at rather low concentrations which are intended to minimize the incidence of various skin problems, such as infections. It would seem more logical and desirable to add antimicrobial properties to a cosmetic than to incorporate agents of questionable activity and value. Excellent examples of the use of anti-bacterial agents are found in baby oils, creams or lotions to help control and prevent impetigo and miliaria; in deodorant preparations to prevent the bacterial decomposition of perspiration; and in scalp products to destroy organisms associated with seborrhea.

Some of the more commonly proposed or used antimicrobial agents in cosmetics are hexachlorophene[40], bithionol, 8-hydroxyquinoline, various cationics consisting of quaternary ammonium morpholinium and pyridinium compounds[41], and antibiotics, such as tyrothricin, and neomycin[42]. Since one of the most notable contributions to the successful treatment of certain skin conditions in recent years concerns the use of antibiotic agents, it will not be surprising if these agents find greater application in cosmetic formulations.

Various phenyl mercuric salts are used either as preservatives or active components of formulations[43]. Spoor[44] has reviewed the agents used against organisms associated with seborrhea and Lubowe[45] recently reported on the effectiveness of a number of anti-dandruff agents, including bis-lauryltrimethylammonium polythionate.

New antimicrobial agents are constantly being presented to the cosmetic chemist for evaluation. Various derivatives of salicylanide, including tetrachlorosalicylanilide[46] and a synergistic mixture of several brominated salicylanilides[47], have been suggested for use in cosmetics. Glyceryl triacetate[48] and monomethylol dimethylhydantoin[49] have also been suggested for use in cosmetic formulations. Decamethylenebis-(4 aminoquinaldinium acetate) has recently been incorporated in a popular mouthwash.

Agents affecting skin pigmentation

Cosmetics may be designed to make the cutaneous surface appear lighter by physical means and by inhibiting pigmentation or bleaching the pigment after it has been deposited. The most commonly used agents for skin bleaches and lighteners, such as red mercuric oxide, ammoniated mercury, and mercurous or mercuric chloride, have been reviewed[50]. Ascorbic acid preparations or natural products containing ascorbic acid, such as lemon juice, have been used, but they are not as effective as the mercury compounds. Monobenzyl ether of hydroquinone interferes with the formation of melanin by blocking the conversion of tyrosine to DOPA. It has been used successfully in the treatment of patients with increased melanin pigmentation, such as freckling, but the incidence of sensitivity is a factor which may limit its use[51].

Dihydroxyacetone has received widespread publicity recently because of its capacity to stain the stratum corneum giving a sun tanned appearance. It has value also in the cosmetic treatment of various skin pathologies accompanied by loss of pigment, such as vitiligo. Recently, 8-methoxypsoralen has been shown to act as a potent photosensitizer, not only increasing the response of skin to light but altering the wave lengths to which the human skin responds[52]. Although it has been found valuable in the physiologic repigmentation of various types of leukoderma, its uncontrolled use in cosmetic products presents some hazards[53].

A multitude of agents are used as sun screens and to list or discuss all of them would be beyond the scope of this paper. However, Klarmann[54] has recently published an excellent review of these agents.

Vitamins

The skin is often the first indicator of a dietary deficiency of certain vitamins and although such deficiencies can be relieved by the oral administration of vitamins, there is some evidence that for certain skin conditions topical application of vitamins may exert a local pharmacodynamic action[55]. Vitamins A, D, E, biotin, panthenol, and pyridoxine are found in various cosmetic products designed to prevent or combat various skin disorders due to suboptimal vitamin intake, faulty metabolic functioning, aging processes, or irritants.

A recent article reviewed the use of panthenol as a healing agent in cosmetics such as skin creams,

lipsticks, after-shave lotions, and hair preparations[56]. One large company has introduced a complete line of cosmetic products containing panthenol and featuring the advantages claimed for this agent.

Hormones

Various estrogenic substances, such as estradiol, estrone, and progesterone, have been used in cosmetics for about twenty years. When estrogens are applied to normal skin, one sees little effect; but in aged individuals or those who have lost the function of their sex glands, one obtains after a few weeks' application better circulation, improved capillary development and blood supply, and a thickening of the surface epithelium[57].

Masters[58] has demonstrated in his studies on the percutaneous absorption of estrogen that the use of two ounces per month of a cosmetic hormone cream containing 10,000 I. U. estrogen per ounce is safe. A hormone cream or lotion containing the recommended 10,000 I. U. of estrone per ounce is said to cause an increase in water retention and thickness of the cell layers of the epidermis, thus producing an anti-wrinkling effect[59].

There is still considerable controversy among medical experts as to the complete safety and extent of efficacy of cosmetic products containing hormones, such as the estrogens. However, evidence is gradually accumulating to demonstrate that by using a properly formulated estrogen-containing cosmetic with limited concentrations and by restricting the amount applied over a definite period of time, there is a safe and demonstrable cosmetic effect obtained.

Steroids

Corticosteroids are important in the dermatologist's armamentarium and are often used in combination with antibiotics or other therapeutic agents. A well-known textbook in dermatology states that no remedy in dermatologic history has achieved so much with so few adverse effects when applied topically as has hydrocortisone and certain of its analogues[60]. Recent investigations have demonstrated again that external hydrocortisone treatment does not produce any major systemic effects following the use of large amounts over prolonged periods of time[61]. The safety of these compounds, their stability and compatibility with other agents, their widespread usefulness, and the fact that there appears to be no reduction of effectiveness on continued use suggest that such agents may some day find application in certain cosmetic formulations where an anti-inflammatory action is desired.

Antihistamines

The antipruritic action of antihistamine salts may be due to inhibition of the cutaneous nerve fibers which mediate sensations of itch and pain. Because of the severe epidermal sensitization which may result from topical application of these agents, other antipruritic substances are usually used in dermatology[62]. The use of antihistaminics in cosmetics has been reviewed[63], but the skin sensitization and cross-sensitization potential of all existing and newer agents must be examined carefully before they are considered for use in any popular cosmetic formulation[64].

Other topical agents

A number of agents reported to promote cell proliferation and thereby stimulate healing have been advocated for use in cosmetics, and some, such as allantoin and urea, are found in many cosmetic products. Mecca[65] has outlined the usefulness of allantoin and Rattner[66] has reported the efficacy of a cream containing urea in promoting a soothing and healing effect in mild eczematous eruptions comparable to chapped skin.

Cantharides, chloral hydrate, and capsicum are employed as rubefacient agents to stimulate scalp circulation. Selenium and tellurium sulfides have been incorporated into shampoos for the treatment of dandruff. Salicylic acid and resorcinol exert keratolytic and mild antiseptic actions. Zinc phenolsulfonate, aluminum chlorhydroxide complex, and other related metallic salts are valuable as astringents. Menthol affects nerve endings in some unknown way to provide a cooling and antipruritic action. Many other agents too numerous to list here are used for various pharmacological effects in cosmetics.

Cosmetic effect from oral administration of agents

In the treatment of various cutaneous diseases there seems to be more and more attention directed to internal medication. Certain fungus infections are being treated orally with such agents as nystatin and griseofulvin. Lupus erythematosus, a metabolic disorder involving possibly the metabolism of flavinoids related to riboflavin, has been relieved by the administration of certain antimalarial drugs which correct this biochemical defect. Psoriasis, also, is felt to be associated with improper lipid metabolism and is being treated with oral medication. Tranquilizers are used in the management of dermatoses associated with increased nervous tension, such as atopic dermatitis, pruritus ani, and psoriasis. Oral enzymes are given for a systemic anti-inflammatory action in various acute and chronic dermatoses.

Many agents affecting metabolism, hormone balance, bacterial invasion, and local blood supply are now administered internally and it is entirely possible that some of these systemic agents will have an important effect on certain cosmetic problems such as perspiration odor, skin dryness, excessive dandruff, balding, and even aging of the skin. Indeed, the acceleration of tanning has already been made possible

by the use of the psoralen compounds. Also, recent studies have indicated that certain anticholinergic agents, such as hexamethonium bromide, isopropamide, methantheline bromide and diphemanil methylsulfate, can be used with moderate success in treating hyperhidrosis[67,68].

We must echo again, however, the warning that when one administers agents orally for a cosmetic purpose, the potential hazards of untoward systemic side effects must always be understood. When oral cosmetics are developed, they must be proved completely safe.

Conclusion

The use of various botanicals, biologicals, antimicrobials, agents affecting skin pigmentation, vitamins, hormones, steroids, antihistamines, orally administered products, and other agents which possess pharmacological activity and exert a cosmetic effect have been briefly reviewed.

The value of many of these agents in the restoration and maintenance of a healthy integument is unquestioned. Many standard therapeutic procedures in dermatology, however, are still used on an empirical basis and the pharmacology of numerous topical drugs is not entirely understood. Similarly, some agents used in cosmetics today are also employed empirically and their exact mode and extent of action need clarification. Until such time as definitive clinical proof is presented either supporting or debunking the claims for such agents, it may be best to avoid hasty conclusions.

Most cosmetic chemists will agree, however, that no real progress is possible in such challenging cosmetic problems as skin aging until we know more about the metabolism of the skin and how it changes with age. The development of new topical pharmacological agents and cosmetic concepts is dependent upon our knowledge of protein chemistry, enzymology, and cellular physiology. The creation of superior cosmetic products, therefore, requires the cooperation of many specialists and the free exchange of accumulated knowledge.

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The Fixative Properties of Musks

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General considerations relating to the chemical structure of products with a musk-like odor

THERE ARE MANY PRODUCTS with a musk-like odor used at present in the perfume industry. The more usual may be classified, with respect to their chemical structure, as illustrated in the accompanying table.

Other musk-like products have been mentioned in the literature. The most extensive study on the subject is undoubtedly that by Beets[1].

When considering the various chemical structures from which products having a musk-like odor are produced one is faced with too much contradictory data to permit drawing any conclusions on the interrelationships between chemical structure and musk-like odor. Nevertheless, some general remarks are possible.

1. Musk-like odor is observed with products having a molecular weight of 14 to 18 carbon atoms. This is surprising enough since within this range many molecules have little or no odor.

2. With most chemical structures, one finds that the molecule is polysubstituted (a fused nucleus may be considered as representing a disubstitution).

All such products with a musk-like odor are products having a low vapor pressure.

When using products having this physical characteristic one is certain that their presence will contribute to the formation of the odor, and not only of the heart, but also of the end-odor of the perfume.

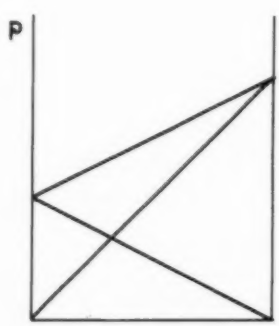
But it is both possible and imperative to question whether such products:

1. have an influence on the head-note of the perfume;
2. will act as fixatives with respect to constituents having a high vapor pressure.

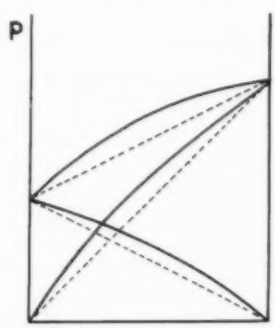
Obviously, the evolution of the odor of perfume is a function of the relative volatility and concentrations of its constituents, but, with such a complex product as a perfume, the laws of evaporation are inextricable.

However, the examination of these laws for far less complex mixtures such as binary mixtures may give some indication both on the enhancement of odor and on fixation phenomena.

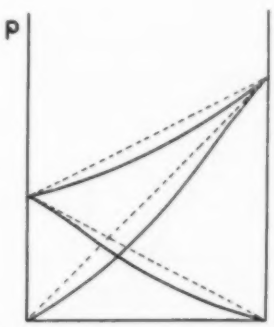
Let us consider a binary mixture consisting of two products A and B and let us assume that the vapor released at ambient temperature and atmospheric pressure has the behavior of a perfect gas (a legiti-



Curve N° 1



Curve N° 2



Curve N° 3

mate supposition, since the concentration in products of the atmosphere over the surface of the liquid is very low.)

The tendency of constituents to evade solution, i.e. their fugacity, is known to occur because their partial vapor pressure is:

1. proportional to the vapor pressure of the constituents;
2. proportional to the molar concentration of the constituent in the mixture;
3. dependent on the cohesive forces between molecules A-A, B-B and A-B.

When the cohesive forces are identical, the mixture is said to be "perfect" or "ideal" and, in this case, one may write the following equation:

$p_A = p^\circ_A X$ and $p_B = p^\circ_B (1\text{-}X)$ (Raoult's Law)

wherein X represents the molar concentration (see Curve No. 1) and p°_A and p°_B represent the vapor pressures.

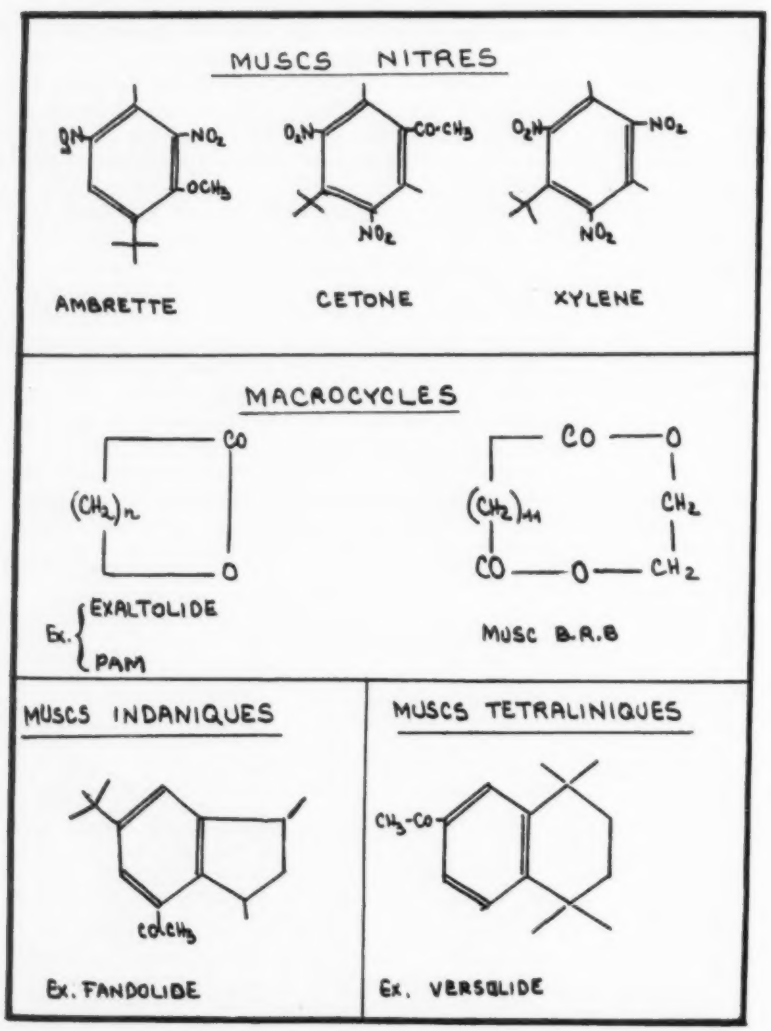
Perfect binary mixtures are rare; in most cases, the cohesive forces between the two constituents are different and, in this case, the above equation becomes:

$p_A = p^\circ_A X \gamma_A$ and $p_B = p^\circ_B (1\text{-}X) \gamma_B$

wherein γ is a coefficient deduced by thermodynamic reasoning. Its value may be higher or lower than 1.

Where γ is higher than 1 (see curve No. 2), the tendency to evading the solution is greater than that of the pure constituent. This phenomenon is attributed to the fact that the cohesive forces between A-B are lower than those of A-A, for example. This tends to prevent miscibility in any proportions, and the molecules of constituent A tend to assemble and to stand apart from the molecules of constituent B.

Where γ is less than 1 (see curve No. 3) the tendency to evading the solution is not as great as with the pure constituent. In most cases, this is due to



The most usual musks

molecular associations or to combinations within the solution.

Let us now attempt to translate this from terms of physics into terms of perfumery. For purposes of simplicity, let us assume that we are in the presence of binary mixtures consisting of an odorus product and of products with little or no odor.

As the case may be, and from the above data, we may either observe enhanced odor (this might be the case when the odorous product is poorly soluble) or decreased odor characteristics. However, in this case, since there is less tendency to evading the solution, the evaporation and, consequently, the odor, will be longer lasting.

It is then possible to say that there is improved fixation of the mixture.

Finally, it should be noted that the cohesive forces between the various products dissolved depend as much on their function as on the overall structural configuration of the molecule.

It is therefore useful, not to say indispensable, to think not only in terms of odor but also of structural configuration, since two products having similar odors but extremely dissimilar chemical structures may very well have different behaviors in an odorous mixture. Such is particularly the case with various musks.

Carrying out a few tests with musks

From the above data, it is readily apparent that a whole series must be conducted in order to confirm such theoretical considerations.

Where musks are concerned, we attempted to find whether these products possessed fixative properties on odorous products having a higher vapor pressure.

Assuming that fixation resulted from a molecular association, we experimented with a mixture of homogeneous chemical constitution having a Rose-like odor. In other words, all the constituents of said mixture consist of products having a primary alcohol function. Why an alcohol function? Because alcohols are capable, through their hydrogen, to form—theoretically at least—molecular associations through "hydrogen bridge" with the functional groupings of various musks, e.g.:

with NO_2 – CO – Esters – Etheroxyde

The mixtures experimented had the following composition:

–Composition with a Rose-like odor	96 p.
–Musk	4 p.
	100 p.

The composition having a Rose-like odor consisted of:

Geraniol	300
Citronellol	300
Phenylethyl alcohol	300
Nerol	100

Each musk-containing mixture was examined, on a smelling strip, after various times of evaporation.

For each olfactory test, the odor was compared to the odor of the rose-like composition which contained no musk, and also to the odor of the corresponding musk.

Three persons were used for these tests. The results obtained are shown in the accompanying table.

What conclusions may be drawn from such data?

First, the various musks, used under the precise conditions described above for the experimentation, possess some fixative properties.

Generally, except for musk xylol, after nine hours the odor of musk is predominant over the rose-like odor.

On the other hand, it is unquestionable that the "rose-like musk" qualification is incomplete, for the very reason that the tone of the musk-like odor is different from one musk to the other.

Finally, it is apparent that after ten minutes of evaporation any of the musks investigated already exerts an influence on the odor.

Reference

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Products investigated	Odor observed after the following time of evaporation				
	10 minutes	3 hours	24 hours	48 hours	96 hours
Rose composition	Rose	Rose	Rose	?	—
Rose + Musk Xylol	Modified Rose	Modified Rose	Musk-like Rose	Musk-like Rose	Musk-like Rose
Rose + Musk Ketone	Modified Rose possibly musk-like	Musk-like Rose	Musk-like Rose	Musk-like Rose	Rose-like Musk
Rose + Musk Ambrette	Slightly musk-like Rose	Musk-like Rose	Rose-like Musk	Rose-like Musk	Rose-like Musk
Rose + P A M	Musk-like Rose	Musk-like Rose	Rose-like Musk	Rose-like Musk	Rose-like Musk
Rose + Musk B R B	Slightly musk-like Rose	Musk-like Rose	Rose-like Musk	Rose-like Musk	Rose-like Musk
Rose + Versalide	Slightly musk-like Rose	Musk-like Rose	Rose-like Musk	Rose-like Musk	Rose-like Musk

Use of Ion Exchange Resins in Antiperspirant-deodorant Preparations

FOR EIGHT YEARS Rohm & Haas Company sponsored research and clinical work on the therapeutic value of ion exchange resins under the direction of the late Dr. Francis M. Thurmon. Under investigation was the utility of the hydrogen form of Amberlite XE-64, a cation exchange resin having carboxy groups as the functional portion. This resin acts as an acid buffer system for maintenance of skin health, through the control of the pH of the normal acid-mantle[1]. A number of metallic salts of this resin were also examined as a treatment for mycotic skin infections[2].

Dr. Thurmon also investigated Amberlite XE-87, a four component mixture of cation and anion exchange resins which consists of a stoichiometric mixture of weakly and strongly acidic and basic ion exchange resins in a micropowdered form, for its effect in treating skin eruptions by means of sequestering, not only the irritant (such as urushiol in posion ivy infections), but also the acidic and basic exudants resulting from the skin eruption[3].

The use of Amberlite XE-64 as an antiperspirant-deodorant[4] is another of several dermatological uses to which the ion exchange resins were applied. The result of Dr. Thurmon's work is a series of case histories, annotating the application of ion exchange resins to dermatological problems, a number of patents of medication formulation, and several articles in dermatological journals[5].

Dr. Thurmon reported 55 clinical histories involving the use of deodorant, antiperspirant compositions containing a weakly acidic corboxylic type ion exchange resin. Because these cases concerned only individuals with histories of intolerance to, or ineffectual use of, commercial preparations without reference to control data, his findings, while dramatic, are not conclusive. Scientifically controlled experimentation is required before a full evaluation of the efficacy of these preparations can be made. Nonetheless, the histories themselves are an interesting harbinger of the great advances which will soon be made in the formulation of deodorant, antiperspirant compositions.

The cosmetic problems arising from excessive axillary perspiration and attendant objectionable odors, were successfully, indeed dramatically, solved by topical application of a cream formulated with Amberlite XE-64. A few of the more interesting case histories follow (commonly accepted generic descriptions have been substituted for brand names of commercial preparations).

Much of the material in this article was compiled from the reports of the late Dr. Francis M. Thurmon, Chief of Clinic, Department of Dermatology and Syphilology, Boston Dispensary, a Unit of the New England Medical Center, and the Department of Dermatology, Tufts College Medical School, Boston, Massachusetts. This work was supported by an Amberlite Ion Exchange Resins Fellowship from the Rohm & Haas Company, Philadelphia, Pennsylvania.

Sex: Female **Age:** 38 **Occupation:** Secretary

History and Examination: This woman developed axillary sensitivity in eleven known instances to topically applied antiperspirant-deodorant preparations. A zirconium-type commercial cream irritated in one day. An aluminum sulfamate-type cream irritated the first time applied. Usually she could use such a product three or four days, then it became irritative and she would switch to another. At times, the dermatitis was severe and days were required for its subsidance. No antiperspirant or deodorant could be applied directly after shaving without producing an irritative inflammatory reaction. She bathed daily and applied the axillary preparation. When going out in the evening this process was repeated. She had developed sensitivity to eleven different commercial preparations; the effective components of these formulations run the gamut of most of the active ingredients in common use. For three months she has used the Resin-Deodorant Cream, at least once daily, and after immediately shaving the axillae, without irritation, odor, perspiration, or damage to fabrics.

Sex: Male **Age:** 26 **Occupation:** Purchasing Agent

History and Examination: This man had a systemic background of seborrheic dermatitis. Since the age of nine years he had suffered recurrent attacks of dermatitis of the face, axillae, pubis, and genito-crural folds. On one occasion he was hospitalized for a generalized and secondarily infected eruption which included the axillae. Organisms, cultured were staphylococcus albic, and aureus (coagulare positive) and alpha enerococcus. Cultures for fungi were negative. His axillae perspired freely and there was odor. The axillae were intolerant to many antiperspirant-deodorant preparations. A commercial preparation containing an antibiotic as active ingredient, a hexachlorophene-type stick and an aluminum sulfate-type spray had produced axillary dermatitis. He tolerated the 25% Resin Powder XE-64 as an axillary therapy three weeks. Subsequently, for four months he used the Resin-Chlorhydrol (20%) Cream as a daily axillary application with complete comfort and effectiveness.

Sex: Female **Age:** 18 **Occupation:** School Girl

History and Examination: This girl was keenly embarrassed from excessive axillary perspiration and odor. Practically all of her dresses became ruined through axillary moisture. A commercial preparation containing a proprietary active ingredient used locally produced a dermatitis. A zirconium-type cream, used after axillary shaving, produced localized and irritative papulitis. She used the Resin Chlorhydrol Cream (11%) once daily, even more often, and immediately after axillary shaving. There was no irritation. Although the axillary perspiration was not controlled completely, it was reduced to a greater extent than by any antiperspirant-deodorant previously used. Axillary odor ceased to be problem.

Sex: Male **Age:** 67 **Occupation:** Pharmacist

History and Examination: This pharmacist, on three occasions developed axillary dermatitis to aluminum sulfate-type commercial preparations. Ten to twenty-one days were required to clear the inflammation. He always had to wait one day after axillary shaving before applying a deodorant lest the axillae become inflamed. He has used the Resin-Chlorhydrol Cream daily for months without irritation, and with complete control of perspiration and odor. He used the 11% chlorhydrol strength mostly, since it was adequate, but for weeks he used daily either the 20% or 26% concentration without irritation, and these concentrations were used immediately after axillary shaving without irritation.

Sex: Female **Age:** 37 **Occupation:** Housewife

History and Examination: This woman had body odor which pervaded the room. This bromidrosis was rank and sickening. She did not use a deodorant because they were irritating. A soap containing both hexachlorophene and a proprietary active ingredient and an aluminum chlorhydrate-type liquid anti-perspirant had caused axillary irritation. She was nervous, tired, had dermatitis herpetiformis of eighteen months duration, and perspired freely. She used the Resin-Chlorhydrol (20%) Cream with good effect, without irritation, for eight weeks daily after bathing, and requested an additional supply.

Of the 55 cases contained in the report, there are no instances of failure to produce satisfactory results from the use of the cream, although only partial success is noted in one or two cases. The histories report the failure of many types of commercial antiperspirants and deodorants prior to the patient's appeal to Dr. Thurmon for assistance.

Aluminum salts of strong inorganic acids are frequently used to inhibit the flow of perspiration by application of solutions thereof to axillary sweat pores and to other body areas. Such solutions frequently cause irritation, in some cases producing dermatitis, and attack cellulose fabrics apparently through liberation of strong acid from the salts. Although a logical step was the use of aluminum salts of weaker acids, these proved much less effective in inhibiting perspiration and odor than the salts of the strong acids.

U. S. Patent No. 2,653,902 discloses Thurmon's objective in his study: "It is an object of this invention to provide compositions which will inhibit the flow of perspiration in an acceptable manner and yet be free of the objections to previously proposed compositions."

There have been some cases of skin irritation associated with commercial antiperspirant-deodorant preparations. The industry has fairly well eliminated the destruction of fabric by the compositions, but the antiperspirant and deodorant efficiency of the preparations remains in doubt.

The formulations which Dr. Thurmon used in treatment of his patients were free of irritant side effects and did no damage to clothing. Strips of cotton cloth, rubbed with these compositions and stored for two weeks, showed no significant loss in tensile strength.

One composition was prepared with 10 parts of aluminum phenolsulfonate, 25 parts of finely divided Amberlite XE-64 cation exchange resin, and 65 parts of a hydrophilic base, tinted with a pink dye and lightly perfumed. Formulations based on aluminum chlorhydrol (11-26 percent) were also used as deodorant-antiperspirants.

In place of the stronger aluminum salts, such compounds as aluminum acetotartrate or aluminum citrate may be used in the compositions. The formulations in which these aluminum salts are the sole reactive ingredient are not particularly effective until there is added a cation exchanger exhibiting carboxylic activity. This yields an antiperspirant-deodorant prepa-

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ration which is less irritating to individuals sensitive to a number of existing commercial antiperspirant-deodorant products.

The carboxylic exchange resin should be present in the composition at about 8% to 25% of the total. The aluminum salt of an organic acid should constitute 5% to 25% of the formulation. Preferred mixtures contain 15% to 25% of the carboxylic exchanger and 10% to 20% of the aluminum salt.

These preparations have been unusually effective for their intended purposes. They are stable, non-greasy, non-irritating, non-dehydrating, non-hygroscopic, removable with water, compatible with medication, free from objectionable odors, non-staining, and non-corrosive. They have been found effective in preventing "dress" dermatitis, which is caused by skin contact with some textile dyes, and can be used safely over a considerable period of time.

The degree of efficiency appears to be due not only to the formation of insoluble aluminum compounds and desquamation of skin with resultant decrease in exudation of sweat; but also to the adsorption of various components of sweat. Thus, the materials which, through decomposition or putrefactive action of organisms, cause irritating or malodorous products are effectively removed. For example, in normal sweat, 100 to 160 micrograms per cubic centimeter of arginine, 70 to 90 micrograms per cubic centimeter of histidine, and amounts between 10 and 60 micrograms per cubic centimeter of such amino acids as isoleucine, leucine, lysine, phenylalanine, threonine, trytophane, tyrosine, and valine have been found. Such compounds particularly those which have high nitrogen content, are adsorbed by the compositions in consequential proportions. Such compounds as arginine and histidine, the latter of which yields irritating histamine, can be removed in large measure.

It is reasonable to believe that the compositions are effective by removing materials from which substances with unpleasant properties can be formed. It is also likely that the preparations are peculiarly effective because they control the acidity of the body surfaces to which they are applied. Furthermore, application of these compositions usually brings a distinct sense of comfort to inflamed or diseased areas, yet these Amberlite XE-64 formulations have not been observed to produce chemical venata[6].

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Present status of hydrophile-lipophile balance

BY PAUL BECHER

Chemical Research Department, Atlas Chemical Industries, Inc., Wilmington, Delaware

IT IS NOW MORE THAN TEN YEARS since Griffin[1] advanced the concept of hydrophile-lipophile balance, or HLB. Sufficient time has passed so that it has become necessary, indeed, not merely to define what this quantity is, but much more importantly, to make clear what it isn't.

To be sure, the concept that the balance between the polar and nonpolar portions of a surface-active molecule was of significance in dictating the properties of that molecule is much older; all that Griffin did was to attempt to apply some sort of numerical scale (of necessity, an arbitrary one) to this concept. This was done in terms of an operational definition; in terms of the stability of standard emulsion formulations.

It later became clear that the HLB index, thus defined, could be arrived at from a knowledge of the structure and composition of the surface-active molecule, at least, in simpler cases. It also appeared (and this, in a sense, was a bit of a surprise) that it was possible to introduce the concept of "required HLB:" that is to say, that value of the HLB index which was required to form a particular emulsion system.

What HLB is not—in a rigorous sense—is a measure of the absolute stability of an emulsion. It *is* true, that for an emulsion system of a given required HLB, a particular emulsifier blend of the correct HLB will be the most stable emulsion possible with that particular blend of emulsifiers. But the HLB number does not insure that some other blend of emulsifiers of the same HLB will not produce a more stable emulsion, and, certainly, it gives no information as to the concentration of emulsifier which is required.

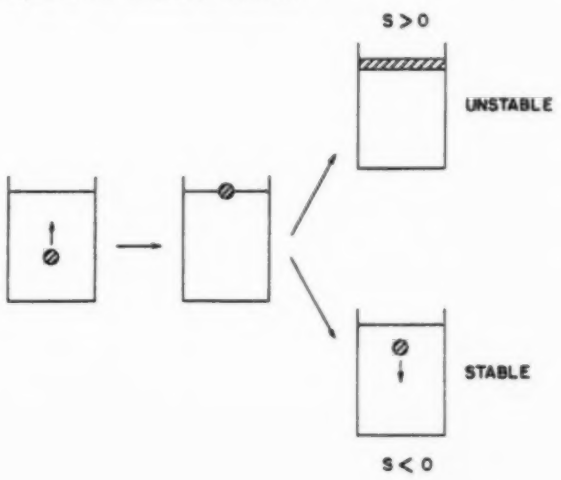
Evidently, then, although the concept of HLB has merit, it does not go far enough in defining the conditions which lead to a stable emulsion.

What is to be done? I think the approach which must be followed is to attempt to correlate HLB with surface properties of the emulsion *system*, rather than just of the emulsifier. This must be done, too, not in any random way, hunting for correlations just for the sake of correlations, but rather in terms of parameters which we know from theoretical considerations must save some connection with emulsion stability.

Unfortunately, this approach has remained unexplored for most of the more than a decade since Griffin's original publication. Only in recent years has a small attempt been made in this direction, and I should like to review at least some of these attempts.

To begin with, let us consider the mutual speading properties of the liquids which make up the emulsion system. If one has a liquid surface and places a drop of another insoluble liquid on this surface, one of two things can happen. In the one case, the droplet will spread out over the surface of the lower liquid; in the second, it will not spread, but remain as a lens-

Fig. 1.—The effect of spreading coefficient on the fate of an emulsion droplet at the emulsion-air interface.



Based on a paper given at the Third Annual National Industrial Pharmaceutical Research Conference. Land O'Lakes, Wisconsin, June 4-7, 1961.

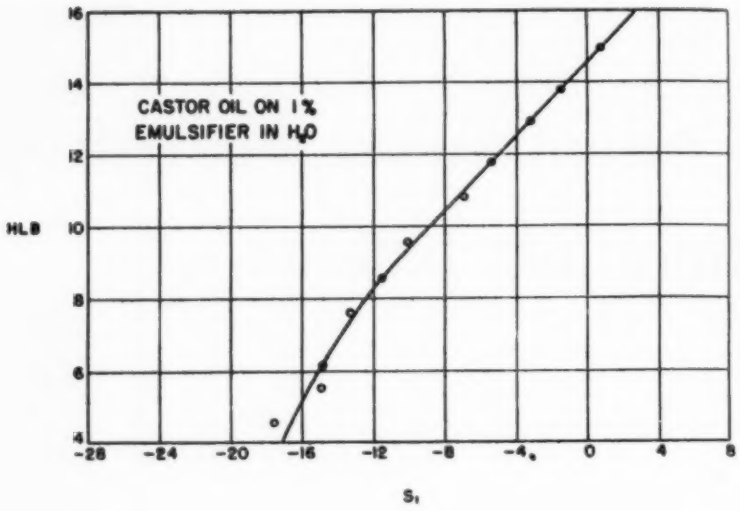


Fig. 2.—The correlation between spreading coefficient and HLB for castor oil and water, for the case of oil-in-water emulsions.

shaped drop on the surface of the substrate liquid. Which phenomenon will occur is governed, as shown many years ago by Harkins, by a quantity called the spreading coefficient. The condition that a liquid A shall spread on a liquid B is given by the condition that the spreading coefficient, defined as

$$S = \gamma_B - \gamma_A - \gamma_{AB}$$

(where γ_A and γ_B are the surface tensions of A and B, respectively, and γ_{AB} is the interfacial tension) shall be greater than zero. Thus, if S is positive, the liquid will spread; if negative, it will not spread.

Now what has this to do with emulsion stability? Let us consider the fate of an emulsion droplet as shown in Figure 1. Imagine that this droplet rises through the emulsion (whether by creaming or as the result of random motion) until it reaches the surface. At this point, one of two things will happen. In one case, the oil drop will spread on the surface and become a film of oil, losing its identity as a droplet. In the other, it will not spread and will, in due course, return to the body of the emulsion. In the first case, of course, repetition of the process leads to the breaking of the emulsion. Clearly then, a negative spreading coefficient is necessary to ensure the stability of the emulsion.

These considerations let H. J. Ranauto and myself at Atlas, and E. S. Chen and S. Ross at Rensselaer Polytechnic Institute[2], to investigate if there was, in fact, some connection between HLB and spreading. This was done by using a series of Spans and Tweens to obtain a range of HLB values of from 4.3 to 15.0. Then, by use of the equation defining the spreading coefficient, we obtained the spreading coefficients for the case of water spreading on the oil and for the oil spreading on the water over the whole range of HLBs and for a large number of oil phases of different chemical characters.

The results for castor oil (Figures 2 and 3) are typical. We find a good linear correlation between HLB and the spreading coefficient for both types of spreading behavior. An extension of the reasoning I have stated earlier leads to the conclusion that the spreading coefficient for the case of an oil-in-water

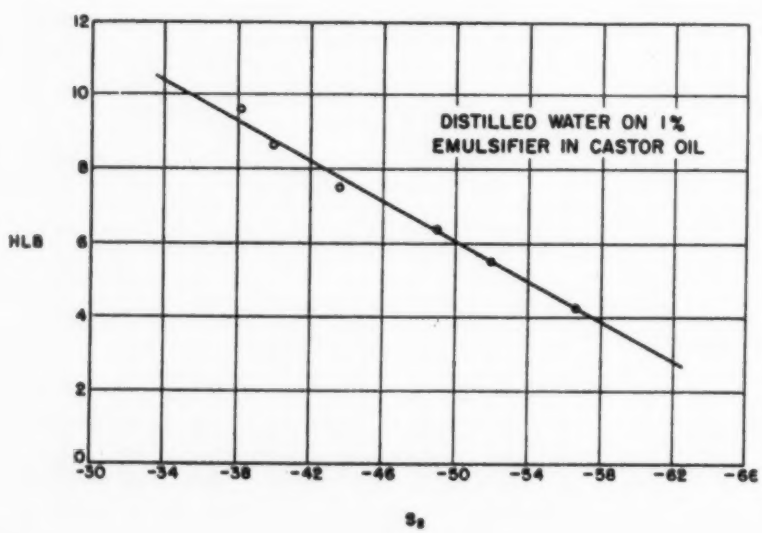


Fig. 3.—The correlation between spreading coefficient and HLB for castor oil and water, for the case of water-in-oil emulsions.

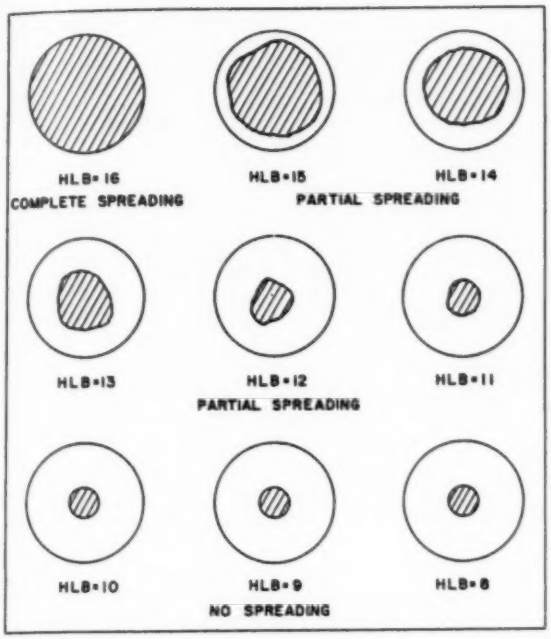


Fig. 4.—Diagrammatic representation of the spreading of toluene on the surface of aqueous solutions of varying HLB.

emulsion (oil spreading on water) must be just barely negative, i.e., of the order of −1, for stability, while the spreading coefficient for the water-in-oil case (water spreading on oil) must be as negative as possible.

It should be noted that the spreading coefficients defined here have been on the basis of 1% solutions of the surface-active agent. Within limits, the spreading coefficient may vary with concentration, and, thus, to a limited extent, we have introduced the concentration of emulsifying agent into a discussion of emulsion stability.

From a practical point of view, it should be pointed out that the spreading process is, after all, physically realizable. Thus, in Figure 4, we show what happens when a drop of toluene is placed on the surface of a series of one per cent solutions of Span 80/Tween 80 mixtures of various HLB. At high HLB, we get complete spreading. As the HLB goes down, the spreading becomes less complete until at an HLB between 10 and 11, the oil drop contracts into the characteristic floating lens. Since the known required HLB for toluene is about 10.5, this behavior is quite satisfactory.

Indeed, this experiment suggests the possibility of a quick, rough determination of HLB by means of such observations, or, indeed, a determination of the possible stability of an emulsion system without recourse to elaborate preparations. Of course, the final refinement of the formulation would still require the preparation of actual emulsions.

Several new approaches have been made by Prof. J. T. Davies of Cambridge University. One very interesting approach has been to treat the HLB number as derived from experimental quantities as something akin to, say, the parachor, and to attempt to resolve the structure of the emulsifier into component groups, each of which makes a contribution (negative or positive) to the total HLB number[3].

The group numbers obtained from the analysis of several known structures (which is precisely the approach used in the determination of parachors) are detailed in Table I. For a given structure, the HLB is calculated by substituting the group numbers of Table I into the relation:

$$\text{HLB} = 7 + \Sigma\,(\text{hydrophilic group numbers}) - \Sigma\,(\text{lipophilic group numbers})$$

where the last term on the right hand side is in general $0.475n$, where n is the number of $-CH_2-$ groups in the lipophile. It should be noted that the $-CH_2-$ groups of the polyoxyethylene chain are *not* included in this total, since each ethylene oxide group is included in the count as a unit.

The results of the calculation of some HLB numbers from these group numbers is shown in Table II, and as can be seen, the agreement is quite satisfactory.

While Davies' equation is based, to some extent at least, on reasonable thermodynamic considerations, it is somewhat naive in its use of nominal structures for the various surface-active agents, since it is well known that the structures given for nonionic agents, especially, are average structures.

Fortunately, there appear to be considerable data accumulating that the behavior of a heterogeneous nonionic agent (all things being equal) is very close to that of the corresponding monodisperse material

TABLE I

Hydrophilic Group Numbers:	
—SO_4Na	38.7
—COOK	21.1
—COONa	19.1
—N (tertiary amine)	9.4
Ester (sorbitan ring)	6.8
Ester (free)	2.4
—COOH	2.1
—OH (free)	1.9
—O—	1.3
—OH (sorbitan ring)	0.5
Lipophilic Group Numbers:	
—CH—	
$-CH_2-$	−0.475
CH_3-	
=CH—	
Derived Group Numbers:	
$-(CH_2-CH_2-O)-$	0.33
$-(CH_2-CH_2-CH_2-O)-$	−0.15

TABLE II

Calculated HLB Numbers

	Experimental*	Calculated
Tween 80	15	15.8
Tween 81	10	10.9
Span 20	8.6	8.5
Span 40	6.7	7.0
Span 60	4.7	5.7
Span 80	4.3	5.0
Glycerol monstearate	3.8	3.7
Span 65	2.1	2.1

* ATLAS values

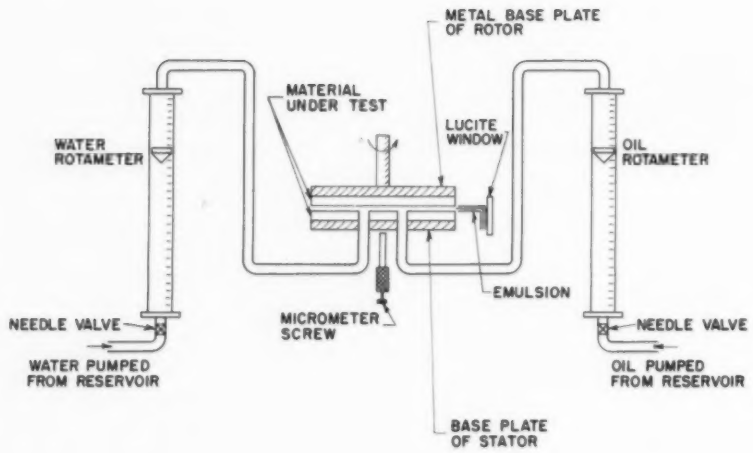


Fig. 5.—Colloid mill for the study of emulsion inversion, according to J. T. Davies.

of the same average composition[4]. If this is the case, the use of Davies' group numbers is thoroughly justified.

Davies has also devoted some attention to the possibility of measuring the HLB of surface-active agents by means of simple experimental measurements of properties related to emulsion stability[3].

For example, he has applied the technique of the measurement of coalescence kinetics first devised by Cockbain and McRoberts[5] to this problem. In Figure 5, we have represented the experiment which is involved.

For the determination of the rates of coalescence of a particular oil-in-water system, the set-up on the left is used. An oil droplet is injected into the aqueous side of an oil-water interface, whereupon it rises to the interface. However, it resides in the interface for an appreciable time, before it actually coalesces with the bulk oil phase. The time it takes is a function of the nature of the oil phase, and the nature and concentration of the emulsifying agent. For the study of water-in-oil emulsions, the inverse experiment, diagrammed on the right-hand side, is performed.

What is actually obtained in this experiment, it should be pointed out, is a range of coalescence times, but the average, or better, median value of a large number of determinations turns out to be quite reproducible. These residence times of the droplet at the interface are, of course, inversely proportional to the rates of coalescence of the emulsion.

With these experimental preliminaries out of the way, let us consider the factors which control the rate of coalescence. For an oil-in-water emulsion, Davies supposes that the coalescence rate, $Rate_1$, may be represented:

$$Rate_1 = A_1 \exp\left[(-0.24\psi_0^2 - \theta \Sigma E_h)/RT\right]$$

where A_1 is a kinetic collision factor, ψ_0 is the double layer potential arising from charges at the interface (very small in the case of nonionics), θ is the fraction of interface covered with molecules of surface-active agent, and E_h is the dehydration energy for the transfer of a hydrophilic group from the aqueous to the nonaqueous phase (quite large in the case of nonionics).

Conversely, the coalescence rate for a water-in-oil emulsion is given by:

$$Rate_2 = A_2 \exp\left(-2n\,\theta\,300/RT\right)$$

where A_2 is again a collision number, n is the number of $-CH_2-$ groups in the lipophile, θ has the previous significance, and 300 is approximately the energy per $-CH_2-$ group for transfer from the nonaqueous to the aqeuous phase.

Combining these two equations, we get

$$Rate_2/Rate_1 = (A_2/A_1)$$
$$[\exp(0.24\psi_0^2 + \theta\Sigma E_h - 600n\,\theta)/RT]$$

Davies argues that the value of the ratio of the coalescence rates is what dictates the *type* of emulsion formed. Thus, remembering that the average lifetime of the drop at the interface is inversely proportional to the rate

$$t_1/t_2 = Rate_2/Rate_1$$

(where t is the average lifetime of the drop at the interface) we can say that an O/W emulsion will be formed if

$$t_1/t_2 = Rate_2/Rate_1 >> 1$$

and a W/O emulsion will occur if

$$t_1/t_2 = Rate_2/Rate_1 << 1$$

If we choose a model system for investigation in such a way that $A_2 = A_1$, the theoretical relationship for the ratio of the rates can be shown to have a formal analogy to the relation between HLB and group number presented earlier, and we get the final result

$$\ln(Rate_2/Rate_1) = 2.2\,(HLB - 7)$$

Since the ratio of the rates is directly obtainable from the drop lifetimes, and θ can be estimated from

interfacial tension data, the HLB can be readily determined experimentally.

A further consideration, based on the energies involved in the transfer of the portions of the molecules across the oil-water interface leads to the additional result

$$\text{Rate}_2/\text{Rate}_1 = (c_w/c_o)\ 0.75$$

where c_w and c_o are the equilibrium concentrations of emulsifier in the aqeuous and oil phases, respectively and the ratio is nothing more than the well-known distribution coefficient.

This finally results in

$$\text{HLB} - 7 = 0.36\ \ln\ (c_w/c_o)$$

which represents another experimental technique for the determination of HLB.

Furthermore, these latter results should be recognized as the quantitative expression of the classical Bancroft's rule, which states that the phase in which the emulsifier is more soluble will be the continuous phase of the emulsion.

It should perhaps be necessary to point out that the considerations presented here in terms of coalescence kinetics are closely related to the spreading properties discussed earlier.

Another aspect of HLB has recently been investigated by Davies; namely, the effect of the hydrodynamic factors[6].

To this end, Davies has constructed an elaborate colloid mill, in which the liquids are continuously sheared between flat discs, as shown in Figure 6. The two phases are metered into the mill separately, and the relative rates can be regulated, thus enabling one to vary the phase ratio continuously. The emulsion is thrown against a lucite window, and the nature of the emulsion (i.e., O/W or W/O) is determined by the wetting or nonwetting of the window.

Thus, in a matter of a few minutes, it is possible to determine the phase ratio leading to inversion. Since, in view of the considerations discussed earlier, this must be connected with the HLB, a relation must exist between HLB and the inversion ratio. That this is indeed the case is shown in Figure 7.

By a slight modification of the experimental technique, this apparatus can be used to determine the required HLB for an unknown oil.

It should be noted that this result is consistent with earlier work in our laboratory where we showed (by a different technique) that the phase ratio at inversion was a function of the particular emulsifier used and not, as earlier theories predicted, dependent only on the laws of solid geometry, but also on the *concentration* of the emulsifier[7].

It is this latter fact which suggests that the continuous emulsifying device of Davies may yet lead us to a better understanding of the effect of emulsifier concentration; indeed, may show (as our previous work suggests) that HLB is somewhat dependent on concentration.

Recently, Ross[8] has shown that there exists a correlation between the logarithm of the critical micelle concentration and the HLB, within chemical groups. Actually, in view of the known relationship between the logarithm of the c.m.c. and the ethylene oxide mole ratio,[9] and between the ethylene oxide mole ratio and HLB, this result is not too surprising.

I have said nothing about factors which do not obviously fit into the broad concept of HLB; for example, the effect of the mechanical properties of the interfacial film on emulsion stability. Such factors are being studied actively in our laboratories. Davies has begun a study of the effect of the materials of construction of the emulsifying machine, which may be simply done by changing the shearing plates of his HLB machine.

And what of the future? Figure 8, perhaps, gives one indication where the future lies. It is an IBM card—the hallmark of our civilization. However, this particular card contains about one-eighth of everything we know about Tween 21. We have many such cards, covering a wide range of emulsifiers.

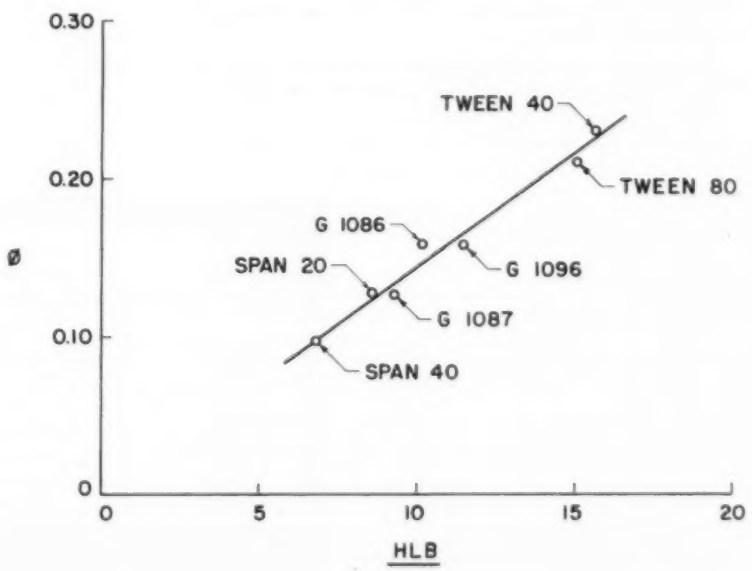


Fig. 6.—Relation between inversion phase volume and HLB.

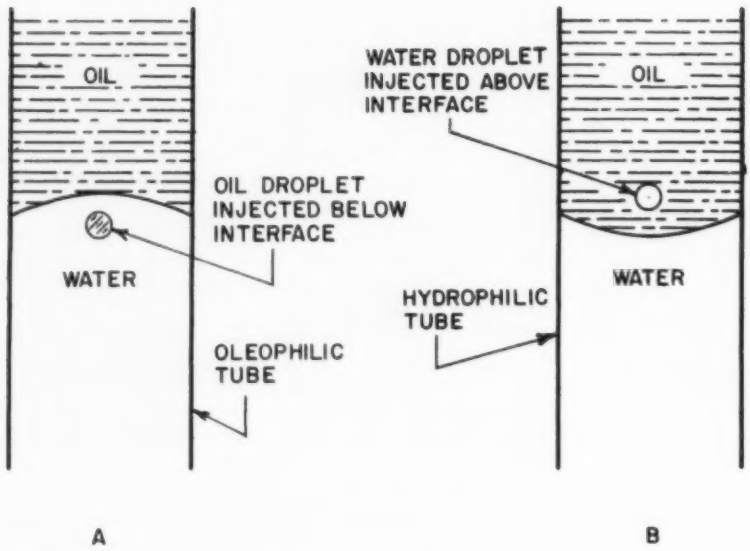


Fig. 7.—Diagrammatic representation of the measurement of coalescence phenomena. (A) For oil-in-water systems. (B) For water-in-oil systems.

Such a collection of punched cards serves two purposes.

The first—and most obvious—is in the realm of information retrieval. Instead of picking up the phone and asking, "Hey, Bert, what's a good emulsifier for—" what shall it be? "—artichoke oil?" we ask the IBM machine instead. The IBM machine really doesn't know as much as Bert does, nor does it have his charm, but on the other hand, the IBM machine is right down the hall, and Bert, through the exigencies of company operations, may well be in Texas—or in Hong Kong!

Second, since this is a rather clever machine (not too bright, of course, but not moronic either), we may ask the machine, "Tell me, is there a correlation between the stability of pine oil emulsions and the weight fraction of lipophilic carbon in the molecule?" And in a few minutes, the IBM machine types out a correlation chart.

We have a group working at getting this kind of data on the punched cards, and soon we hope to be in a position to ask these kinds of questions.

At this time, it is certainly not clear if we will be able to incorporate data of these types into the HLB pattern. Quite probably not—and we may have to modify or abandon this mode of description. On the other hand, we have shown that HLB is related to important physical properties of the emulsion system. We have been justified in employing this useful guidepost in the past, and should still find it valuable in the immediately, foreseeable future.

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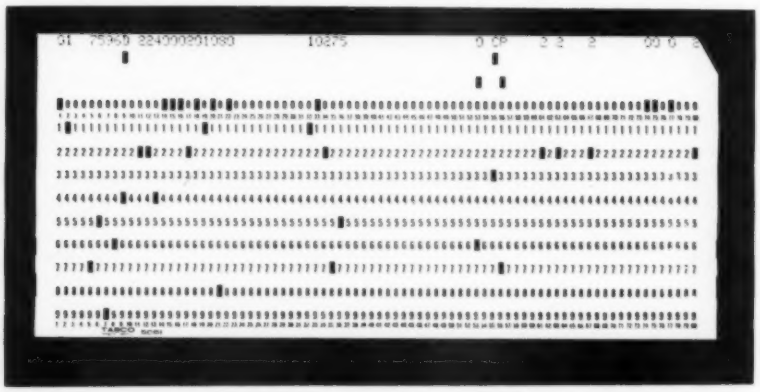


Fig. 8.—The future of HLB research? This IBM card contains approximately one-eighth of everything we know about Tween 21.

Activated carbon adsorbs essence to recapture dwindling market

BY DR. MURRAY BERDICK, Evans Research and Development Corporation, New York City

Recent patented process

1. **permits economical shipping; reduces customs costs**
2. **keeps essence in stable form during transport**
3. **reconstitutes product on site**
4. **reclaims dwindling export business**
5. **improves product quality**

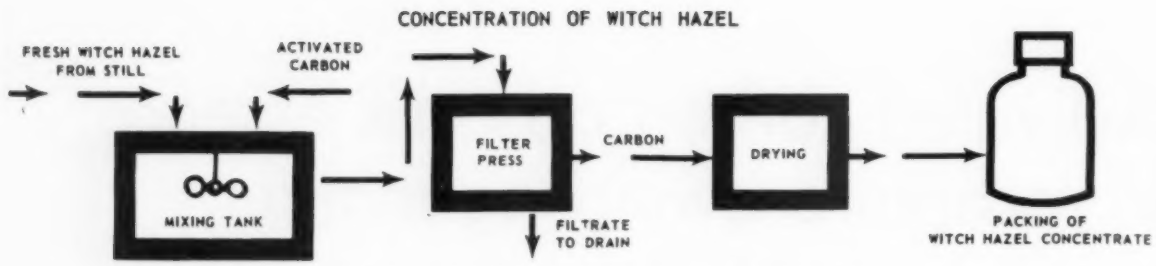
A PATENT COVERING A NEW PROCESS for extracting the active principle of witch hazel and then reconstituting it has stemmed the tide of a dwindling export market and now exports are on the rise again. Witch hazel, the common form of which is more properly known as "Hamamelis Water," has been an old standby in the medicine chests of America for generations, and, in various related forms, was a favorite remedy of the American Indians for at least 200 years, and probably longer.

The distilled witch hazel extract became so well known and widely used during the past century that it was shipped to many parts of the world, although the only commercial source was a small area, principally in Connecticut, where the American shrub, *Hamamelis virginiana*, grows in sufficient profusion to permit it to be used economically in the extraction process. For a number of years, production for the entire world has been carried on in three plants, all of which are located in Connecticut. In recent years, there has been a considerable shrinkage of the market abroad because increasing costs of shipping and rapidly rising import duties in many countries have made it impossible to export the product profitably.

The shifting emphasis of modern medicine is clearly illustrated by the fact that the United States Pharmacopeia once listed four different products derived from Hamamelis, and the National Formulary at various times has listed three of these. In the most recent editions, no Hamamelis product is listed in the U.S.P., and only Hamamelis Water is official in the N.F. The 25th edition of the U. S. Dispensatory still describes five Hamamelis products:

1. *Hamamelis (the dried leaves).*
2. *Dry extract of Hamamelis (made by drying alcoholic extract).*
3. *Liquid extract of Hamamelis (made by percolating Hamamelis leaf with 45% alcohol).*
4. *Ointment of Hamamelis (from the liquid extract, wool fat, and paraffin).*
5. *Hamamelis Water N.F. (from an aqueous distillate of Hamamelis twigs, diluted alcohol).*

Other known products are Hamamelis bark (listed in the U.S.P. until 1916); semi-solid extract of Hamamelis (partially evaporated alcoholic extract of leaves); Hamamelis solution (a distillate from leaves macerated in water and alcohol); tincture of Hamamelis (percolated from bark in alcohol, then diluted



Schematic shows concentration process for concentration of witch hazel

with water); and Hamamelin (precipitated by water from an alcoholic extract of leaves).

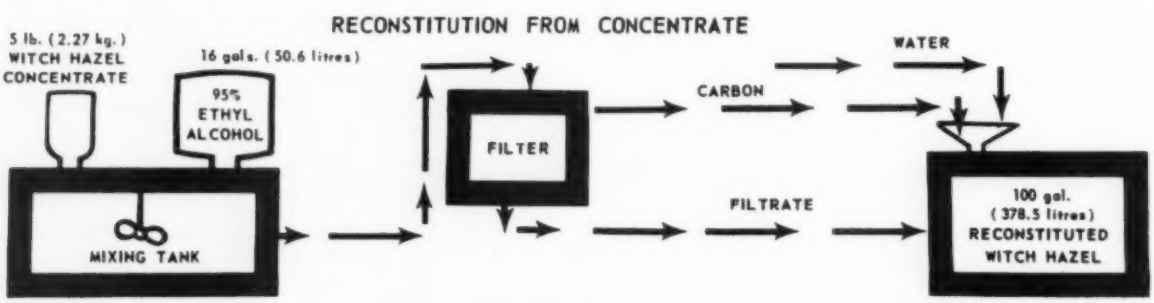
One of the three manufacturers of witch hazel is United Witch Hazel Distillers, Inc., a subsidiary of the 100-year-old Humphreys Medicine Company. In 1953, a new management decided to do something about the shrinking foreign market for witch hazel. Although many previous attempts to produce an acceptable concentrate which could be reconstituted into Hamamelis Water had come to naught, Humphreys placed the problem in the hands of Evans Research and Development Corporation in 1954.

By 1955, a process of adsorbing the small amount of active principle on activated carbon, and then eluting the essence with aqueous alcohol had been developed at Evans Research, and a U. S. Patent application was filed. When the patent was granted in 1959 (U. S. Patent 2,897,115), Humphreys started commercial use of the process, and by 1961, was successful in recapturing a substantial portion of the South American market.

The concentration process is shown schematically in Figure 1 and the reconstitution process is shown schematically in Figure 2.

Since the adsorbate is a stable form of the essence, the reconstituted product is the equivalent of conventional witch hazel and often superior to witch hazel which has been subjected to adverse conditions during shipping. The reconstituted witch hazel meets all the specifications of the National Formulary.

Aside from the improvement in quality which is achieved, the savings in shipping and customs charges are substantial, and an expansion of this commercial application to new markets abroad is now being undertaken.



The reconstitution process

Research Techniques in the Flavor Field

by James A. Rogers

Instrumental analysis had aided the flavor chemist in providing basic information regarding the constituents of citrus oils, their stabilities and odor correlations. For many years we have used infrared spectra to measure the initiation and degree of spoilage of these oils and the resulting off-flavor.

Several of the components responsible for the infrared bands have been separated and identified as oxidation products of terpenes, and their origin determined. Lemon and lime oils follow similar patterns in spoiling; orange oil follows a somewhat different path. Concentration of the stable oxygenated components, and thus the natural antioxidants, is the most practical method to prevent spoilage in the natural oil, although other attempts have been made.

A qualitative and quantitative study of these concentrated oils by instrumental techniques has aided reconstitution of flavor formulations using essential oil isolates or synthetic derivatives. Such compounds are more flavorful and stable materials than the oil itself.

Liquid C-18 Saturated Acids Derived From Linseed Oil

J. P. Friedrich, H. M. Teeter, J. C. Cowan and G. E. McManis, Northern Regional Research Laboratory, Peoria, Ill.

Liquid C-18 saturated monocarboxylic acids that fail to crystallize at −70°C. have been prepared from linseed oil, linolenic acid, and tung oil. Heating one part of linseed oil in three parts of glycol (weight-volume ratio) at 295°C. for 1 hr. with 25% excess sodium hydroxide, followed by distillation and hydrogenation of the resulting free fatty acid monomers and separation of the straight-chain components by low temperature crystallization from acetone, yielded these liquid acids. The relative proportions of cyclic acids, straight-chain monomeric acids, and polymer varied with the type of starting material and with the conditions employed. Cyclic acids in excess of 30% yields were obtained from linseed oil. Some hydroxylation of the fatty acids apparently takes place during cyclization; the amount increases with ascending temperatures, as evidenced by a rise in polyester content of the polymer fraction. Thru *J. of the American Oil Chemists Society*, 38, No. 7, p. 329, July (1961)

Antibacterial Activity of Benzalkonium Chloride in the Presence of Cotton and Nylon Fibres

by G. E. Myers and Carole Lefebvre.

The antibacerial activity of benzalkonium chloride in aqueous solution and as a tincture has been studied. The test organism Staphylococcus aureus F.D.A. 209 was exposed to the action of benzalkonium chloride for varying intervals of time in the presence and absence of cotton and nylon fibres. The disinfectant was neutralized immediately at the end of the exposure time by transferring the test organisms to Letheen broth and subsequent subculture on blood agar medium. Under these conditions cotton fibres in a concentration as low as 4% w/v adversely influenced the antibacterial activity of 1:5000 and 1:10,000 aqueous solutions of benzalkonium chloride. The adverse effect increases as the amount of cotton fibre increases .The greater the concentration of bacteria the more likelihood of survival in the presence of germicide containing cotton fibres. Concentrations of cotton fibre up to and including 4.8% w/v did not adversely effect a 1:1000 tincture of benzalkonium chloride or a 1:1000 aqueous solution. Nylon fibre in concentration up to and including 5% w/v did not adversely affect the antibacterial activity of 1:1000 or a 1:5000 aqueous solution of benzalkonium chloride. Thru *Scientific Section, Canadian Pharmaceutical Journal*, *94*, p. 55, No. 7, (1961)

Germ. 1,107,222: Synthesis of Dihydrojasmone

Council of Scientific and Industrial Research (New Delhi) 12.5.59 as 12o, 25.C.18983 (25.5.61)

Dihydrojasmone is prepared by condensing an alkylmethylketone with succinic esters in the presence of tert. butyl potassium, (b) converting the resulting half ester into paraconic acid by means of hydrobromic acid and acetic acid (c) pyrolysing the latter cpd. and (d) cyclising the product. Thru *Derwent Organic Patent Bulletin*, *246*, Germ. Gp.5-p. 3, June 23, 1961.

Bactericidal Activity of Formaldehyde Vapor

Importance of the Presence of Moisture on the Bactericidal Action of Formaldehyde, Rao V., *Indian J. Pharm.* 22:258 (Oct.) 1960. Dept. of Pharm. Andhoa Univ. Waltair, India.

Bactericidal activity of formaldehyde vapor, passing through powders contaminated with B. subtilis spores, decreased as the relative humidity varied from 98 to 65%. The death rate of the organisms depended upon the quantity of formaldehyde in the moist vapor passing through the powder per minute. Formaldehyde vapor in varying concentrations by diln. with moist air did not indicate any reduction in activity, but diln. of formaldehyde vapor with dry air considerably reduced the death rate. It was further found that certain optimum moisture content is essential for efficient bactericidal activity. Thru *Am. J. of Hospital Pharm. 18*, No. 6, p. 370, June, 1961.

Panthenol Aerosol Hair Spray U.S. 2,983,650.

Issued May 9 to Saul Howard Rubin, Nutley, N. J. assignor to Hoffman-La Roche Inc. also Nutley.

A liquid composition for dispensing on the hair under pressure as an aerosol comprising panthenol in an alcoholic solvent and liquefied fluorinated hydrocarbon gas propellant. Thru *Aerosol Age*, *6*, No. 7, p. 73, 1961.

Testing and Evaluation of Pharmaceutical Flavors

by R. A. Phillips

A use profile method is suggested to be used in preliminary formulation of pharmaceutical flavors. Four methods of masking are discussed: matrix, complementing, drowning, and diverting.

Flavor technique is considered under these headings:

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use of sweet, sour, salt, and bitter as masks; neutral base plus bouquet; change in non-active moiety of drug itself; solubility effect; texture; body as viscosity and as flavor; astringency; lingering flavors; effervescence; floral, nut, meat, vegetable, pickle, culinary flavors in pharmaceuticals; effects of color; blenders and smoothers; fixatives; anesthetics; insoluble colloids as a tool; hot and cold products; nondescript flavor; two-phase products; extemporaneous mixes.

The Role of Plastics in Packaging of Dry Pharmaceutical Products

by C. B. Burnside

A comparison in use of plastics for packaging dry pharmaceutical products as direct substitute for glass, steel, aluminum, paperboard, or other materials. Described in detail are the product protective qualities of plastics in such areas as moisture vapor transmission, product protection against breakage as a result of resiliency of the plastic, and light resistant properties of plastic when compared with other standard packaging materials, such as flint and amber glass.

Stressed is the importance of establishing product performance specifications by the product development man. They then may be accurately interpreted by the package development man to provide the optimum packaging materials for insuring adequate product protection and product quality.

Accounting for Tastes

by David R. Peryam

A review of relevant background information on sensory testing with primary emphasis on laboratory experimentation, showing special problems encountered and the value of statistical approaches to their solution. Statistical methods for dealing with some of the basic problems are discussed.

Emphasis is placed on the importance of experimental design, which both demands that an experiment be properly planned and permits accurate interpretation of the results. How some common techniques are used with typical problems is demonstrated by examples. Analysis of variance and the use of factorial designs is considered of special value for controlled laboratory experiments.

Design of a Human Skin Test

by Jack I. Northam

The designs used in some earlier tests on human skin for the evaluation of the efficacy of various compounds are reviewed. The Latin Square principle in the design of experiments is discussed, and then applied to an assay problem of evaluating topically applied steroids for comparative anti-inflammatory activity. The advantages of the use of a well-designed experiment are enumerated.

Physiology and Psychology of Flavor

by Warren F. Gorman, M. D.

Flavor is a compound sensation, composed chiefly of smell, but also of taste. And in the chemical sense, as well as tactile, kinesthetic, thermal and psychic factors, is distinctive in that particles from the external environment must enter the organism to permit flavor perception. Flavors that are generally acceptable have the characteristics of familiarity, associations with other pleasurable phenomena, safety and physiologic acceptabil-

ity, but social and psychological pressures alter these characteristics.

Smell perception is extremely sensitive, being stimulated by a concentration of 10^{-13} molar. Olfactory acuity is diminished by drugs which reduce food intake, and a serious loss of olfactory acuity is found in over 26% of older people.

The chemical sense is defined as recording stinging, acrid or burning sensation in the mucous membranes of the body, responding to chemical agents being incorporated into the subject and producing reflex secretory activity such as salivation.

Taste sense perceives the 'primary' tastes of sweet, salt, sour and bitter, but blending of these tastes does not produce a taste spectrum. Congenital diminution of taste occurs, similar to color blindness, and may be inherited as a dominant or recessive characteristic.

Problems in Masking Modern Pharmaceuticals

by Fred Wesley

Pharmacists in product development are facing pressure exerted from opposite directions; one is public demand that medicine be tasteful, the other is extreme obnoxiousness of most modern pharmaceuticals. This dilemma has remained unresolved mainly because certain of its causes rarely had been examined. To bring it closer to eventual extinction a thorough study of some of its facets was undertaken which showed the existence of technical, procedural, physiological, psychological, economic, educational, and organizational problems. The less known ones are described.

The Use of Cab-O-Sil as a Suspending Agent

by J. M. Plaxco, Jr.

Cab-O-Sil, a colloidial silica compound of high purity, extreme fineness and enormous surface area, appeared to offer promise as a pharmaceutical suspending agent. The comparative ability of Cab-O-Sil to suspend calamine, zinc oxide, magnesium carbonate, bismuth subnitrate, bismuth subcarbonate, sulfur and kaolin was determined.

Papers Presented before the Scientific Section of the American Pharmaceutical Association, April 23-28, 1961

The Antifungal Activity of Some Amides of o-Coumaric Acid.
By H. Wayne Schultz. Oregon State College School of Pharmacy, Corvallis, Oregon.

A series of anilide derivatives of o-coumaric acid were prepared. These compounds were studied for their inhibitory activity against pathogenic fungi. A corresponding series of salicylanilide derivatives were also tested against these organisms. The relationship of chemical structure was analyzed.

The Pharmacology of 3-Phenyl-1,2,4-Triazole.
By C. J. Erdman, W. R. Gibson, J. W. Martin and D. B. Meyers, College of Pharmacy, Butler University, Indianapolis, Indiana.

The 3- phenyl derivative of 1,2,4-triazole showed the unique property of producing strong C.N.S. stimulation when injected i.v. into mice, rats and rabbits and a pronounced depressant activity when administered i.p. into

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the same animals. Orally it gave good protection against electroshock in rats. In all species studied it lowered blood pressure and relaxed isolated smooth muscle. Significant inhibition of both cholinesterase and monoamine oxidase by the compound was demonstrated.

Effects of Processing on the Rheology of Thixotropic Suspensions.

By T. H. Simon, H. G. DeKay and G. S. Banker. Purdue University, School of Pharmacy, Lafayette, Indiana.

A study has been made of suspensions in water of bentonite USP and Veegum HV in various concentrations, processed by an agitator with a marine-type propeller, an Eppenbach Homo-Mixer, a Tri-Homo Disperser and a Manton-Gaulin two-stage homogenizer. Each of the above pieces of processing equipment was operated at several shear rates or shear loads. Evaluation of the suspensions involved the plotting of rheograms by a fully automated Ferranti-Shirley Cone-Plate Viscometer and the subsequent determinations from these rheograms of yield value, coefficient of plastic viscosity, thixotropic area and spur value. The results obtained indicated that differences in rheological parameters caused by different processing rates and equipment were such that their consideration in the formulation and development of thixotropic suspensions is warranted.

The Stability of Bacteriological Preservatives in Parenteral Solutions I. Factors Influencing the Loss of Antimicrobial Agents from Parenteral Solutions in Rubber Stoppered Containers.

By L. Lachman, S. Weinstein, G. Hopkins, S. Slack, P. Eisman and J. Cooper, CIBA Pharmaceutical Products Inc., Summit, New Jersey.

Losses of preservative due to degradation and absorption from rubber closed multi-dose vials were investigated. The preservatives evaluated were benzyl alcohol, phenylethyl alcohol, p-chloro-β-phenylethyl alcohol, chlorobutanol and methyl paraben. The elastomer closures used in this study were intended to be representative of those most commonly employed for pharmaceuticals and were natural, neoprine and butyl rubbers. The temperature dependency of the degradation and diffusion processes were studied. An attempt was made to correlate preservative loss and microbiological activity.

The Influence of Non-Equilibrium Sample Temperature on the Stability Predictions Extrapolated from Elevated Temperature Studies.

By Morton Scott, Warner Lambert Research Institute, Morris Plains, N. J., and Leon Lachman, CIBA Pharmaceutical Products Inc., Summit, N. J.

Storage of samples for stability evaluation in elevated temperature ovens may cause errors in the assay results for individual samples, if heating and cooling effects are ignored. For usual kinetic studies, however, groups of samples are placed in the oven at one time and individual samples are removed for analysis at designated time intervals. Theoretical and experimental considerations are presented, indicating that in the case of first and pseudo first order reactions each of the samples in the group is subjected to the same degree of error. Rates of degradation calculated from a series of such samples are identical to that obtained under ideal conditions of instantaneous heating and cooling. Consequently, decomposition rates obtained under the usual oven storage conditions, where lags in heating and cooling times exist, give useful information for estimating product stability.

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News of the Societies

SCC cosmetic seminar set for Sept. 26-27

Some 13 aspects of Biological Activity in Cosmetics will be discussed by as many speakers at the 8th annual cosmetic seminar of The Society of Cosmetic Chemists scheduled to convene Tuesday and Wednesday, September 26 and 27 at the Barbizon Plaza Hotel, New York City. The following program has been planned for the two-day event.

Tuesday, September 26

8:00-9:00 A.M. **Registration**

9:00 **Introductory Remarks.** H. W. Zussman, program chairman

Session 1. Paul Lauffer, Ph.D., moderator

9:20 **Anti-inflammatories.** Norman Orentreich, M.D. (N.Y. University School of Medicine)

10:00 **The use of fluorides in anti-cariegenic dentifrice.** D. S. Barrie (Proctor & Gamble)

10:40 **Should sunscreens be incorporated into cosmetics?** John M. Knox, M.D. (Baylor University College of Medicine)

11:20 **Enzymes.** K. L. Howard, Ph.D. (Wallerstein Laboratories)

12:45 Luncheon: New York Academy of Sciences 2 East 63d Street

Session 2. Everett Saul, Ph.D., moderator

2:10 P.M. **Effects of estrogens on sebaceous glands.** John Strauss, M.D. (Boston University School of Medicine)

2:50 **Pregnenolone acetate, a dermatologically active steroid.** John Silson, M.D. (Revlon)

3:30 **Vitamins.** S. H. Rubin, Ph.D. (Hoffman LaRoche)

4:10 **Anti-cholinergics.** J. F. Migliarese, Ph.D. (Colgate Palmolive)

5:45 Cocktails: New York Academy of Sciences, 2 East 63d Street

6:30 Dinner

Wednesday, September 27

Session 3. H. W. Zussman, moderator

9:00 A.M. **Antibiotics.** Vincent de Gennaro and R. E. Mackay (Chas. Pfizer & Co.)

9:40 **Should bacteriostats be added to toilet soaps?** W. M. Linfield, Ph.D., and R. E. Casely (Armour & Co., Grocery Products Division)

10:20 **Skin-bacteriostat relations.** Thomas Furia (Geigy Industrial Chemicals)

11:00 **Mechanisms of bacteriostatic action.** Eugene D. Weinberg (Indiana University)

11:40 **The open problem of biological activity in cosmetics.** Emil Klarmann (Lehn & Fink)

12:45 Luncheon: N. Y. Academy of Sciences 2 East 63d Street

Hazelton to address Los Angeles chapter

Dr. Hazelton

Dr. Lloyd W. Hazelton, founder and president of Hazelton Laboratories, Falls Church, Va. is scheduled to address the Sept. 18 meeting of the Los Angeles chapter of the Society of Cosmetic Chemists in Rodger Young Auditorium, Los Angeles.

Dr. Hazelton has been an active member of the SCC since 1952, and a frequent speaker at the national meetings. The firm which he heads is engaged in consultation, research and development in the biological sciences.

He received his B.S., M.S. and Ph.D. degrees from the University of Washington, majoring in pharmacy and pharmacology. He has been an instructor in Pharmacology and a Professional Lecturer at Georgetown University School of Medicine, and has held assistant and associate professorships at George Washington University School of Pharmacy.

Much of his time is spent on problems relating to color additives for use in foods, drugs and cosmetics under the new Color Additive Amendments.

—by **E. A. Walker,** Publicity Chairman

New York Chapter hears legal status

The legal status of the cosmetic chemist in his company affiliation was discussed at the Sept. 13 meeting of the New York Chapter of the Society of Cosmetic Chemists.

A lively discussion on the rights and viewpoints of the individual and of management opened the first of fall-winter meetings. Legal advisors were guest speakers, and a spirited question and answer period followed. The dinner-meeting was held in the Regency Room of the Hotel George Washington. —by **R. K. Lehne,** Publicity Chairman

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PRESSURIZED PACKAGING (AEROSOLS). By Alfred Herzka, Jack Pickthall. Although technical problems occur with all types of packages, those which arise with pressurized packages are many and complex. This reference book, by two recognized authorities deals with propellants, containers, valves, filling methods, laboratory procedures, emulsified systems, and perfumes. There is a complete section containing more than 200 formulations, including foods, insecticides, cosmetics, paints, and numerous other products. 400 pages. Illustrated. Price $15.00.

PERFUMERY SYNTHETICS AND ISOLATES. By Paul A. Bedoukian. This carefully compiled volume meets the genuine need for authoritative data on perfumery synthetics. It embraces the history, chemistry, physical and chemical properties, manufacture, uses, and other pertinent data of the principal perfumery compounds; and covers the important perfumery synthetics. A complete index adds to the value of this important work. 488 pages. Price $10.25.

THE HANDBOOK OF SOLVENTS. By Leopold Scheflan and Morris Jacobs. The most useful work of its kind today. Part I covers theoretical aspects and practical attributes such as solvent action, solvent power, evaporation and evaporation rates. In Part II the physical constants of over 2700 liquid compounds are tabulated for easy comparison. 728 pages. Illustrated. Price $12.00.

COSMETICS—THEIR PRINCIPLES AND PRACTICES. By Ralph G. Harry, discussed the skin, its nutrition and scientific care: the hair, its proper grooming, the physio-chemical problems involved in its washing; the teeth and their care, covering the present status of different dentrifices, and the luster-producing properties of ingredients. Much of the information has its source in the research activities of its author, embracing chemistry, dermatology, and microbiology. 786 pages. Illustrated. Price $17.25.

INTERNATIONAL ENCYCLOPEDIA OF COSMETIC MATERIAL TRADE NAMES. By Maison G. deNavarre, brings you reference data you will turn to constantly . . . the most complete listing of all the materials of the world used in cosmetic manufacture . . . including quick concise descriptions of approximately 4,000 materials . . . the names and addresses of the suppliers . . . and a very useful cross-index of the materials and their uses. You will use it when seeking new materials, or substitutes for those you may now be using. 400 pages. Price $7.50.

HANDBOOK OF COSMETIC MATERIALS. (Their Properties, Uses, and Toxic and Dermatologic Actions). By Leon Greenburg and David Lester. Contains alphabetical listing, with frequent cross references, of information on approximately 1,000 substances. For each compound gives: formula (including collateral names), properties, toxic action, dermatological action. Exhaustive bibliography. Essential for manufacturing chemists, cosmetic industry, dermatologists, allergists. 467 pages. Price $14.50.

THE ESSENTIAL OILS. By Ernest Guenther, with the collaboration of leading experts, this monumental six-volume work includes: Vol. I, Origin and Development of Essential Oils. 427 pages. Price $9.50. Vol. II, detailed data on several hundred constituents of essential oils. 852 pages. Price $13.50. Vol. III, discusses the oils of the plant families Rutaceae and Labiate. 777 pages. Price $13.50. Vol. IV, covers the widely used oils: citronella, lemongrass, bois de rose, cassia, and others. 752 pages. Price $13.50. Vol. V, takes up other oils of special interest to flavor, perfume and soap manufacturers: rose, ginger, cardamon, anise. 507 pages. Price $13.50. Vol. VI, completes the monographs on individual oils: wintergreen, sweet birch, juniper berries, and the numerous pine oils. 552 pages. Price $13.50.

MANUAL FOR THE ESSENCE INDUSTRY. By Erich Walter. Comprises methods, with formulas for making all kinds of essences for liquors and alcoholic drinks, fruit juices and jams, mineral waters, essences for fruits and other vegetables, essences for confectionery and pastry. Describes raw materials and laboratory practice. Discusses taste and the transfer to foods and beverages. 427 pages. Illustrated. Price $8.25. Published 1916.

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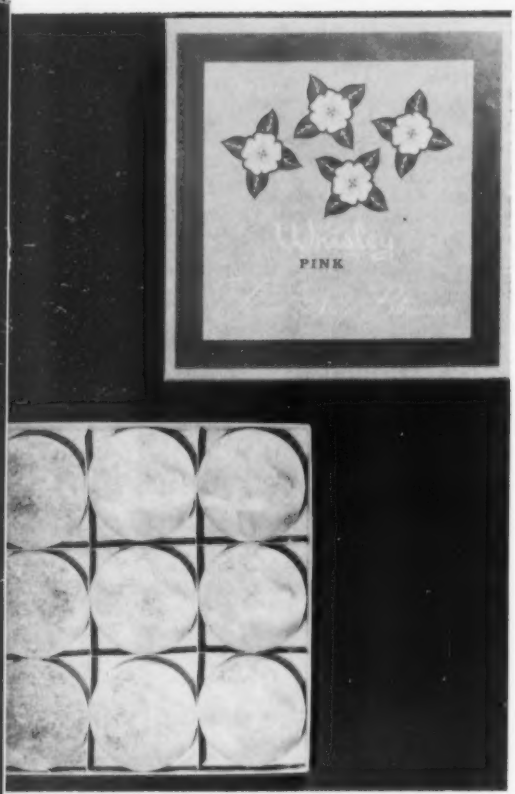

Allen B. Wrisley Co., Chicago has just introduced Soap Blossoms, a new fragrant toilet soap in floral design cakes. Gift packaged, the product is made in colors (pink, maize and turquoise) to match modern baths. Retails at $1.50 for box of nine cakes.

Alberto VO5 Conditioning Creme Rinse has just bowed nation-wide in retail drug and food stores. The product makes "just washed hair" manageable by untangling the snarls that occur after a shampoo. It ends flyaway hair. Product is pale peach in color, and the glass bottle has been designed with etched swirls and a pinched waist. Foil label in maroon, gold, purple and white gives good product identification. The Alberto-Culver Company item (7 oz.) retails for $1.00. Package was designed and produced by Owens-Illinois Glass Company, Toledo, Ohio, and the labels were made by Wheeler-Van Label Co., Grand Rapids, Mich.

Enameled container for 1200 metered sprays of Incanto Cologne is being shown by Simonetta, Inc., New York City. Decoration on the container is a reproduction of a Piranesi etching of the Coliseum. Fragrance is a floral-woody blend, with accents of tabac and oakmoss.

Vitabath contains soapless cleansers, deodorizers, extract of chestnut, vitamins A, B_2, E, F, and Biotin. An item of Nu-Vie Products, New York City, it is packaged in cool lime and bright green plastic squeeze, non-roll, non-slip bottle. Closure is white plastic cap, inside of which measures bath quantity; concave outer section is shower or shampoo quantity. Two new size containers #86 (32-oz.) and #84 (4.2-oz.) have been introduced. Another package in the line includes five .4-oz. yellow and white striped tubes in a bright green box topped with acetate cover with yellow ribbon on opposite corners.

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NEWS & EVENTS

International meeting on allergy set for October

The Fourth International Congress of Allergology will be held October 15-20 at the Commodore Hotel, New York City, with more than 50 specialists from all over the world scheduled to discuss latest findings in allergy research, according to Dr. Bernard N. Halpern of Paris, president of the International Association of Allergology.

Dr. Justin M. Andrews, director of the National Institute of Allergy and Infectious Diseases, Bethesda, Md., will speak on "Research in Allergology" at the first day's session. Other speakers at the opening session will be Dr. Francis B. Rackemann; Prof. Pasteur Valley-Radot of Paris; Dr. William B. Sherman, New York City; and Dr. Halpern.

Some topics on the agenda include Allergic Manifestations, the Role of Pharmacologically-active Substances, Histamine and Serotonin Antagonists, Wandering Cells in Allergy, Physiological Patterns in Allergic Disorders, Contact Dermatitis, Drug Allergy and others.

Krebiozen discussion to highlight perfumery meeting

Dr. Andrew C. Ivy, former head of the department of clinical science, University of Illinois College of Medicine will be the luncheon speaker at The Chicago Perfumery, Soap and Extract Association, Inc. meeting October 10. Krebiozen, the controversial drug for cancer, will be his topic.

Rapid growth of cosmetics and toiletries to continue

Willard Gidwitz, president of Helene Curtis Industries, Inc., Chicago, predicts the rapid growth of his company and the entire cosmetics and toiletries industry will continue.

Speaking before the New York Society of Security Analysts, in late August, Gidwitz said that the industry's sales gains of the last 10 years would be extended by development of entirely new product areas.

He cited foreign markets as an increasingly significant factor, and said,

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"they are only now reaching the growth stage which the domestic market entered 10 to 15 years ago. Industry volume," he continued, "which rose from $840 million in 1950 to $1,784 million last year, could again more than double its volume in the 60's."

Turning attention to his company, Gidwitz said that it will also benefit from large-scale expansion of the Studio Girl house-to-house sales division plus increased participation in the home repair products market. Also from its foreign operations in 80 countries, Gidwitz said that Helene Curtis expects a 30% increase in income this year. "Licensing income should increase to a million dollars from last year's record high of $780,000," he said.

He indicated that the firm's sales of professional products for beauty salons are continuing to grow 8 to 10% a year. He related other industry prognostications to the new aspects of personal grooming and beauty care that are constantly gaining acceptance. Gidwitz said that industry volume could increase at the same rate in the 60's that it maintained in the 50's. "Just as the entire $81 million hair spray market was non-existent only 10 years ago, and the total market for hair products has passed the $300 million mark, so will other new products bring increased expenditures for beauty care and good grooming," he said.

Helene Curtis estimates sales of $66-$67 million for its fiscal year ending February 28, 1962, Gidwitz reported, and this would be an increase of more than 20% from the $54 million of the last fiscal year.

Fredell named to cosmetic committee of AMA

Walter G. Fredell has been appointed assistant secretary to the Committee on Cosmetics of the American Medical Association. Recently engaged in research and development of pharmaceuticals and cosmetics for Warner-Lambert Pharmaceutical Co.,

W. G. Fredell

Fredell previously was associate professor of pharmacy at Drake University and taught at St. Louis College of Pharmacy. He is a registered pharmacist in several states, and is active in the Society of Cosmetic Chemists. He is currently chairman of the society's sub-committee on evaluation of anti-perspirants and deodorants. Fredell is author of a number of scientific papers on cosmetics, a recent one on *Product Information* was published in the June issue of AMERICAN PERFUMER. He is a past president of the St. Louis branch of the American Pharmaceutical Association and of the Society of Pharmacists in Industry.

Six months profits highest in Factor's history

Sales and profits for Max Factor & Co., Hollywood, Calif., for the first half of this year were up 5 and 15%, respectively, over the same period last year, and marked a record high for the firm.

President Max Factor, Jr. reports consolidated net profits for the period ended June 30 were $1,887,458 compared to $1,638,214 for the six months in 1960. Net sales and royalties for

first half of 1961 were $28,510,329. Last year-half sales were $27,269,464.

The firm is now negotiating and has an option to purchase 20 acres of land in the Chicago area. Plans are being drawn for a shipping and warehousing unit comprising some 125,000 sq. ft., and the facility is expected to be ready for occupancy in 1962. Space has been reserved at the site for future installation of manufacturing facilities. Location of the site has not been announced.

Hall named head of Beauty Counselors

The board of directors of Beauty Counselors, Inc., Detroit, has elected George T. Hall president, succeeding Ellsworth R. Beeman who becomes vice-chairman of the Board. J. Paul Kennedy, formerly Hall's assistant, is newly-elected vice president and general sales manager.

Norton S. Walbridge remains as chairman of the board.

Martin moves to general manager of Peggy Newton

George M. Martin has been appointed general manager of Peggy Newton, Westfield, Mass., a wholly owned subsidiary of Stanley Home Products, Inc. Martin has worked

G. M. Martin

closely in the development of the cosmetic line since it was acquired by Stanley Home Products last January. He is a member of the Peggy Newton directorate board.

Hazel Bishop and Lanolin Plus plan merger

Subject to approval of stockholders, Hazel Bishop and Lanolin Plus, Inc. will merge Nov. 1. Hazel Bishop stockholders, under the merger terms, will receive one share in the surviving company (Hazel Bishop) for every four shares held. Stockholders of Lanolin Plus will get one share of the new common stock for each share.

For its fiscal year, ended last Oct 31, Hazel Bishop reported net sales of $7,971,505 and a net loss of $354,000. Lanolin Plus reported sales of $14,000,000 for the fiscal year ended last June 30, clearing $530,000.

Breck sponsors beauty contest in Latin America

The most beautiful girl in Latin America will be chosen next January at a beauty contest in Manizales, Columbia. John H. Breck, Inc. will underwrite its cost as part of a special promotion in Central and South America.

The contest will be held in conjunction with the 8th Annual Manizales Fair. Finalists will be winners of contests conducted in 17 different Latin American countries by Breck distributors.

Included among the prizes is an all-expense-paid trip to the United States, with visits to major cities in this country, plus a complete wardrobe created by Valdiosera, famous Mexican designer and artist.

Jose Marcial, Jr., director of international sales for the company, is co-ordinating the promotion.

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Book on perfume and flavor materials

"Perfume and Flavor Materials of Natural Origin" published by Steffen Arctander, was inadvertently mislabeled in our July issue.

This book, resulting from many years of private and professional study, is the most up-to-date and complete one-volume work dealing exclusively with natural raw materials for perfumes and flavors.

Mr. Arctander is employed by International Flavors and Fragrances of New York City, and is instructor in flavors, perfumery and essential oils at the University Extension Division of Rutgers University, Newark, N. J.

The book, printed in Denmark, is published and distributed by Mr. Arctander at P. O. Box 114, Elizabeth, N. J.

Heart ailment fatal to perfumer Chaleyer

Philip Chaleyer, perfume consultant for Rhodia, Inc. and Hoffmann La Roche Inc., suffered a fatal heart ailment Sept. 7. Chaleyer, a native of Lyons, France, studied at the chemical school there. He served with the French army in World War I at the Dardanelles and in the chemical warfare service. Chaleyer opened his own perfume and essential oil firm in 1928, and previously was associated with Givaudan in Switzerland, England and U. S. He was a member of The American Society of Perfumers, Inc., Essential Oil Association of the U. S., and the Society of French Perfumers.

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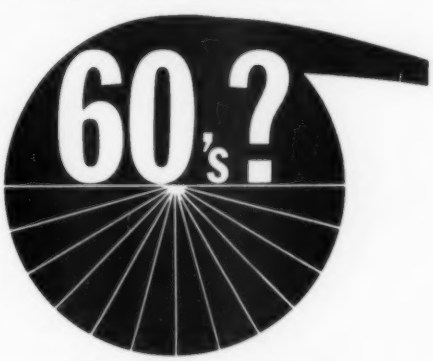

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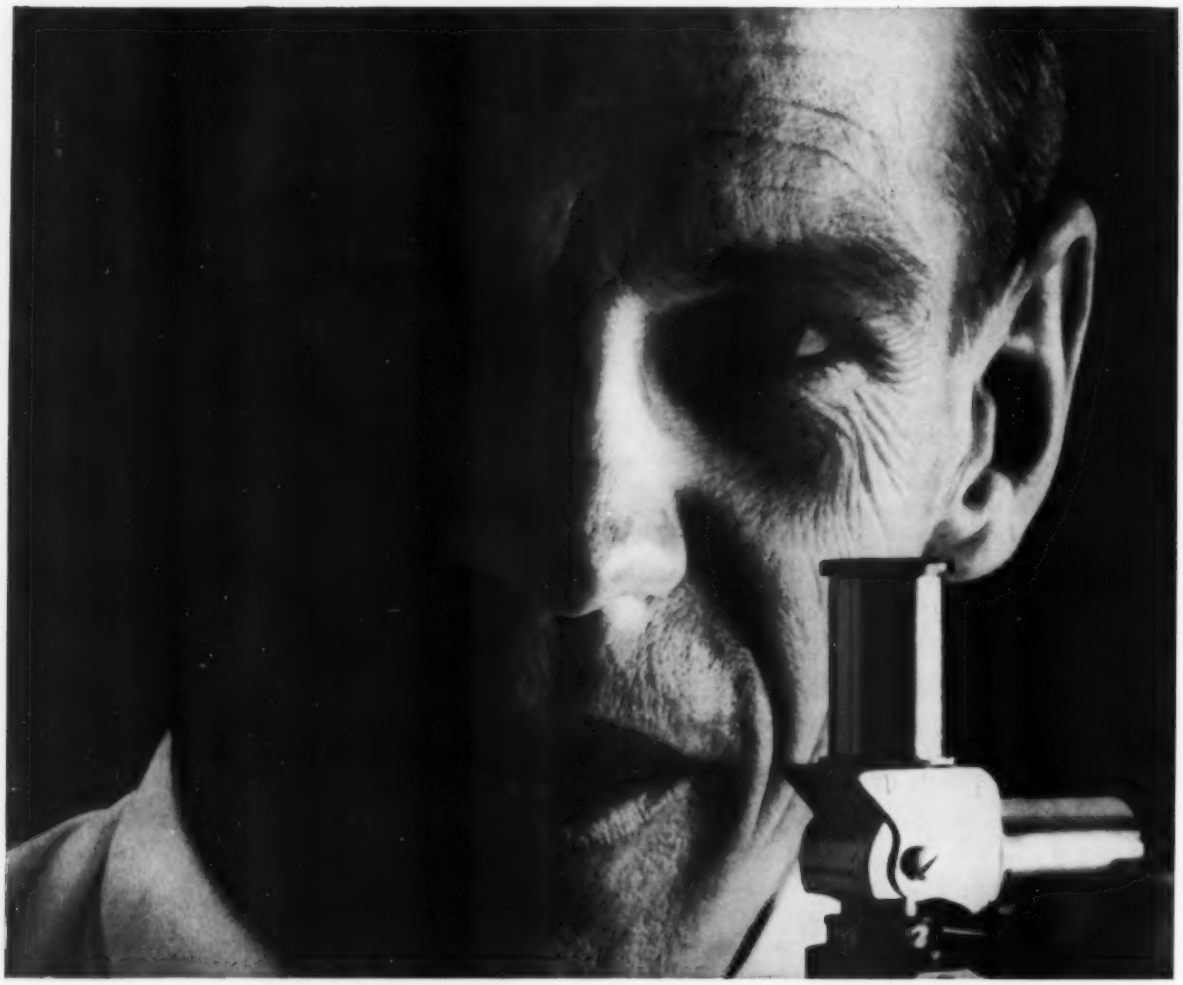

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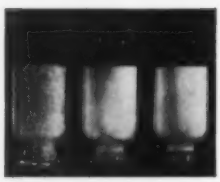

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PERSONALITIES

Charles A. Suter is new president of Geigy Chemical Corp., Ardsley, N. Y. He succeeds **William F. Zipse** who has been elected chairman of the executive committee. Zipse has been president of the firm since 1943 and has had 58 years of service with the chemical producer.

President Suter has been executive vice president since 1950.

Benson Storfer

At the recent sales meeting of Parfums Corday, Inc.—the first as a wholly-owned subsidiary of Max Factor & Co.—**Benson Storfer,** veteran perfumer, was honored on his 50th anniversary in the fragrance industry.

He was presented with a golden scroll signed by all his associates, and a solid mahogany humidor filled with 50 cigars. Storfer was president of the firm for 30 years, having been succeeded by his son, Herbert, just last month. The veteran perfumer is acting in a consulting capacity for the firm.

Richard Y. Kitsuse

Richard Y. Kitsuse has been named director of research and development at F. Ritter & Co., Los Angeles producer of essential aromatics.

Kitsuse, a veteran of more than 10 year in the flavor field and food industry, is a member of the American Chemical Society and the Institute of Food Technologists.

Dr. Kaufman

Dr. Jerome G. Kaufman is new director of chemical research and production at Fleuroma, Inc., Long Island City, N. Y. In his new position, Dr. Kaufman will further integrate the creation of new aromatic chemicals with pilot and plant production.

William C. Freeman is new president of Paul A. Dunkel & Company, Inc., Jersey City, N. J. importer and exporter of gums and specialties. He succeeds **Paul A. Dunkel,** who has become chairman of the board. Freeman has been president of Clarence Morgan, Incorporated, Dunkel's midwest representative, since 1955.

Edwin G. Ross is new controller of Helene Curtis Industries, Inc. Former assistant controller, Ross will continue as assistant treasurer and assistant secretary. He will be responsible for the accounting, data processing, systems and procedures and internal auditing of the toiletries producer and all its subsidiaries.

Jack Rasmussen is newly-appointed manager of mid-west operations for Perry Brothers, Inc., New York City producer of perfume bases, essential oils and aromatic chemicals. He will have headquarters in new Chicago offices at 14 E. Jackson Boulevard.

Mrs. Evelyn E. Bunge, Chicago, has been re-elected president of the National Hairdressers and Cosmetologists Association. Also **Marguerite Buck,** New York City, was elected styles director; and **Ora Randall,** Pontiac, Mich., chairman of the official hair fashion committee.

Obituary

Morris Shapiro, chairman of the board Lucky Heart Laboratories, Inc., Memphis cosmetic manufacturing and distributing company, Aug. 27.

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iso-Propyl linoleate of interest to cosmetic chemist

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INDUSTRY EVENTS CALENDAR

Sept. 26-27—8th Annual **Cosmetics Seminar of The Society of Cosmetic Chemists,** Theatre of the Barbizon-Plaza Hotel, New York City.

Oct. 4-7—International Congress of the Federation of European Aerosols., Lucerne, Switzerland.

Oct. 10—**Chicago Perfumery, Soap and Extract Association,** Luncheon, Sheraton Towers, Chicago.

Oct. 15-20—**4th International Congress of Allergology,** Commodore Hotel, New York City.

Oct. 18—**The American Society of Perfumers,** New York City. (Place to be announced.)

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Oct. 18-20—**23rd Annual National Packaging Forum,** Biltmore Hotel, New York City.

Oct. 31-Nov. 1—**First International Symposium of Automatic Merchandising,** McCormick Place, Chicago.

Oct. 31, Nov. 1-2—**10th Canadian National Packaging Exposition,** Automotive Bldg., Exhibition Park, Toronto.

Nov. 7-10—**Packaging Machinery Manufacturers Institute Conference-Workshop and Exposition,** Cobo Hall, Detroit, Mich.

Nov. 14—**Chicago Perfumery, Soap and Extract Assoc., Inc.,** Annual Thanksgiving Stag Party, Furniture Club of America, Chicago.

Nov. 15—**The American Society of Perfumers,** New York City. (Place to be announced.)

Nov. 27-Dec. 1—**28th Exposition of Chemical Industries,** New York Coliseum, New York City.

1962

May 9—**Scientific Section of the Toilet Goods Association, Inc.,** New York City. (Place to be announced later).

June 24-29—**Joint Convention of the Toilet Goods Association, Inc.** (USA) and the **Toilet Goods Manufacturers' Association of Canada,** Chateau Frontenac, Quebec, Canada.

July 2-5—**The 2nd International Congress of Cosmetic Science,** London, England.

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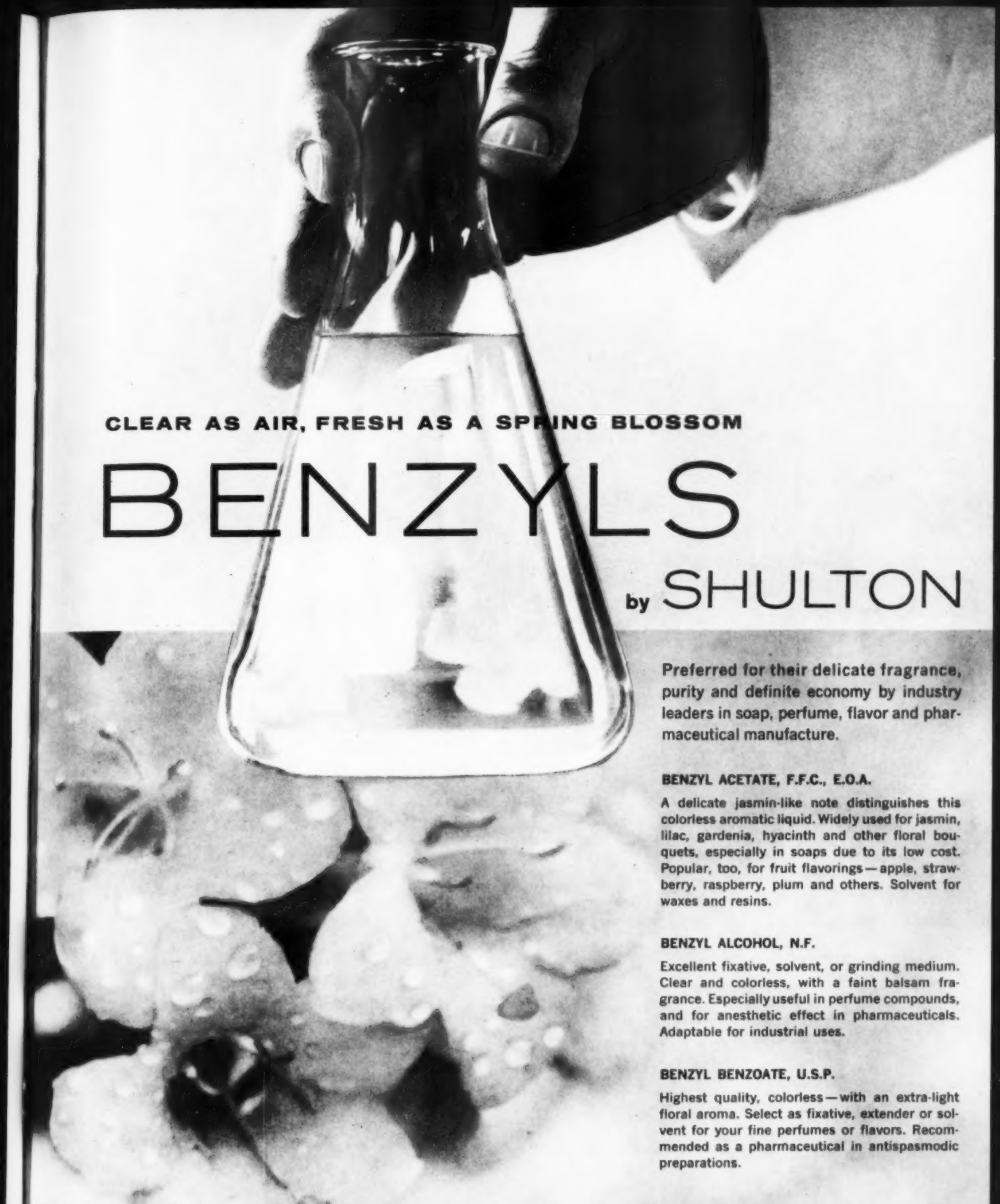

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